(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 1 386 923 A1

(12) EUROPEAN PATENT APPLICATION

published in accordance with Art. 158(3) EPC

(43) Date of publication:
04.02.2004 Bulletin 2004/06

(21) Application number: **02717152.9**

(22) Date of filing: **15.04.2002**

(51) Int Cl.[7]: **C07D 473/16**, C07D 473/18, C07D 473/24, A61K 31/52, A61P 11/06, A61P 17/00, A61P 31/12, A61P 31/18, A61P 31/20, A61P 35/00, A61P 37/02, A61P 37/06, A61P 37/08, A61P 43/00

(86) International application number:
PCT/JP2002/003727

(87) International publication number:
WO 2002/085905 (31.10.2002 Gazette 2002/44)

(84) Designated Contracting States:
AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR
Designated Extension States:
AL LT LV MK RO SI

(30) Priority: **17.04.2001 JP 2001118232**

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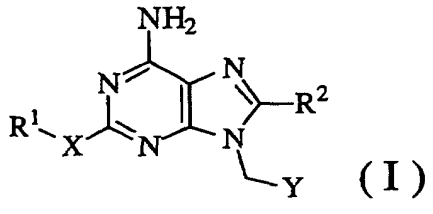
(54) NOVEL ADENINE DERIVATIVES

(57) This invention relates to an adenine derivative, a tautomer thereof, or a pharmaceutically acceptable salt thereof represented by general formula (I):



(I)

wherein X represents NR^3 (wherein R^3 represents a hydrogen atom or C_{1-3} alkyl) or the like; R^1 represents substituted or unsubstituted alkyl or the like; R^2 represents hydroxyl or the like; and Y represents a substituted or unsubstituted aromatic hetero ring or the like. Also, the present invention relates to pharmaceuticals such as an interferon inducer, antiviral agent, anticancer agent, type 2 helper T cell selective immune response inhibitor, antiallergic agent, and immune response modulator comprising the above derivative as an active ingredient.

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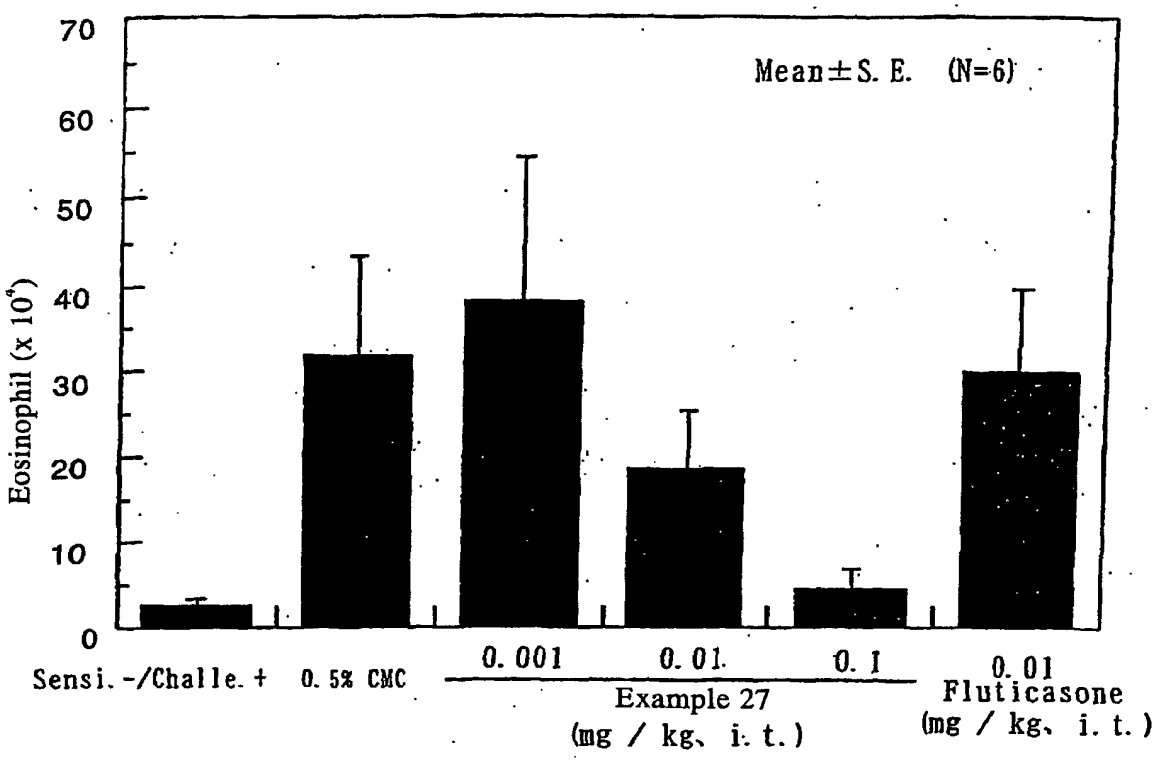
Fig. 1


70
60
50
40
30
20
10
0
Eosinophil (x 10⁴)
Mean±S. E. (N=6)
Sensi. -/Challe. +
0. 5% CMC
0. 001
0. 01
0. 1
Example 27
(mg / kg、 i. t.)
0. 01
Fluticasone
(mg / kg、 i. t.)

Description

Technical Field

[0001] The present invention relates to an adenine derivative that is useful for preventing or treating viral diseases such as hepatitis B, hepatitis C, or AIDS, cancerous diseases, or the like. Also, the present invention relates to a pharmaceutical preparation such as an interferon inducer, antiviral agent, anticancer agent, type 2 helper T cell-selective immune response inhibitor, antiallergic agent, or immune response modulator comprising the above derivative as an active ingredient.

Background Art

[0002] Interferon is one of the most important factors that are in charge of phylaxis or immune modulation. It has been already put to practical use as a therapeutic agent for hepatitis B and C and an immunotherapeutic agent for cancer. In particular, interferon is practically the only therapeutic agent available for hepatitis C. Interferon is a polypeptide having a molecular weight of about 20,000. It is produced by gene recombination or cell culture, and it can be administered only in the form of injection. What is desired is, accordingly, the development of an interferon inducer that can be orally administered.

[0003] Examples of known substances having interferon-inducing activity include double-stranded nucleic acids derived from viruses or other living organisms and high molecular weight polymers such as Poly(I)/Poly(C) or polycarboxylate. Doublestranded nucleic acids or high molecular weight polymers, however, are problematic in, for example, antigenicity, contamination by pathogenic microorganisms or biological stability. In addition, since they has a high molecular weight, development of oral preparations therefrom is difficult. Several substances, such as fluorenones, pyrimidinones, or anthraquinones have been examined as low molecular weight interferon-inducing substances (Mayer, G. D., et al.: Science, 1970, 169, 1214, Nichol, F. R. et al.: Antimicrob. Agents Chemother., 1976, 9, 433, Stringfellow, D.A., et al.: Antimicrob. Agents Chemother., 1991, 15, 111). Because of their low therapeutic effect or toxicity, however, development of pharmaceutical preparations therefrom was relinquished (Reiter, M.A., et al.: J. Leukocyte Biol. 1994, 55, 234). An imidazoquinoline derivative, R-837 (Imiquimod), is known as another low molecular weight interferon-inducing substance (EP 145,340). R-837, however, has low interferon-inducing activity, and the development thereof in the field of oral preparations was no longer performed due to its side effects. The present inventors also found that a specific purine derivative had interferon-inducing activity (WO 99-28321). Since these compounds had low water-solubility, they were not sufficient in terms of gastrointestinal absorption.

[0004] In contrast, helper T cells play major roles in immune responses. There are two types of helper T cells, i.e., Th1 cells and Th2 cells. Examples of cytokines produced upon the activation of Th1 cells are interleukin-2 (IL-2) and interferon-γ (IFN-γ). Examples of cytokines produced from Th2 cells are interleukin-4 (IL-4) and interleukin-5 (IL-5). Th1 cytokines activate macrophages, natural killer cells, or the like, and they are known to be mainly involved with cellular immunity such as phylaxis against viruses or bacteria. Th2 cytokines are involved with humoral immunity such as antibody production from B cells. In particular, IL-4 induces B cells to produce IgE antibodies and has actions of Th2 cell differentiation or proliferation. IL-5 is capable of activating eosinocytes, accelerating differentiation or proliferation, life lengthening, or the like. Accordingly, it often plays a major role in allergic inflammation. In fact, these Th2 cytokines are increased in lesions of patients having allergic inflammation such as asthma or atopic dermatitis with which Th2 cells are mainly involved. Steroid drugs are often used to treat these diseases. However, chronic administration of steroid drugs disadvantageously generates a variety of side effects such as diabetes, osteoporosis, adrenal disorder, or moon face. Since steroid drugs inhibitorily act against both T cells, i.e., Th1 cells and Th2 cells, they may cause infectious diseases as a result of inhibiting Th1 cells. Accordingly, pharmaceuticals that can selectively inhibit Th2 immune responses can be safe therapeutic agents for allergic diseases without causing infectious diseases.

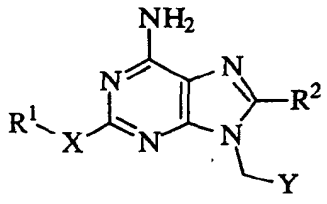
Disclosure of the Invention

[0005] An object of the present invention is to provide a low molecular weight compound with improved physical properties (such as solubility or pharmacokinetics) that are effective for preventing or treating viral diseases such as hepatitis B, hepatitis C, or AIDS, cancerous diseases, and diseases resulting from type 2 helper-T cells and that can be orally administered.

[0006] Under the above circumstances, the present inventors have conducted concentrated studies. As a result, they found that an adenine derivative with a specific structure had excellent interferon-inducing activity, type 2 helper T-cell-selective immune response inhibitory activity, and excellent physical properties. This has led to the completion of the present invention.

[0007] More specifically, the present invention includes the following.

(1) An adenine derivative, a tautomer thereof, or a pharmaceutically acceptable salt thereof represented by general formula (I):



(I)

wherein X represents NR^3 (wherein R^3 represents a hydrogen atom or C_{1-3} alkyl), an oxygen atom, or a sulfur atom; R^1 represents substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; R^2 represents hydroxyl, mercapto, C_{1-8} acyloxy, or C_{2-8} alkoxycarbonyloxy; and Y represents a substituted or unsubstituted naphthalene ring, a substituted or unsubstituted 5- or 6-membered monocyclic aromatic hetero ring containing 1 or 2 hetero atoms selected from the group consisting of nitrogen, oxygen, and sulfur atoms, or a substituted or unsubstituted fused bicyclic aromatic hetero ring containing 1 or 2 hetero atoms selected from the group consisting of nitrogen, oxygen, and sulfur atoms.

(2) The compound according to (1) above, wherein, in general formula (I), R^1 represents C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{2-8} alkoxyalkyl, C_{1-8} hydroxyalkyl, aryl, heteroaryl, aralkyl, or heteroarylalkyl.

(3) The compound according to (1) or (2) above, wherein, in general formula (I), R^1 represents C_{1-6} alkyl.

(4) The compound according to any of (1) to (3) above, wherein, in general formula (I), X represents NH.

(5) The compound according to any of (1) to (3) above, wherein, in general formula (I), X represents an oxygen atom.

(6) The compound according to any of (1) to (5) above, wherein, in general formula (I), Y represents a unsubstituted or substituted pyridine ring or a substituted or unsubstituted pyrazine ring.

(7) The compound according to any of (1) to (5) above, wherein, in general formula (I), Y represents a unsubstituted or substituted naphthalene ring or a substituted or unsubstituted thiophene ring.

(8) The compound according to any of (1) to (6) above, wherein, in general formula (I), Y has 1 to 4 substituents when Y is a pyridine ring, and 1 to 3 substituents when Y is a pyrazine ring at any positions, wherein the substituent is selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, hydroxyl, mercapto, C_{1-4} alkylthio, a halogen atom, amino, C_{2-8} dialkylamino, C_{1-4} monoalkylamino, pyrrolidinyl, piperidino, and morpholino.

(9) The compound according to any of (1) to (6) and (8) above, wherein, in general formula (I), Y represents a pyridine ring which may have a substituent selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, hydroxyl, mercapto, C_{1-4} alkylthio, a halogen atom, amino, C_{2-8} dialkylamino, C_{1-4} monoalkylamino, pyrrolidinyl, piperidino, and morpholino; R^1 represents C_{1-6} alkyl; and R^2 represents hydroxyl.

(10) The compound according to (9) above, wherein X represents NH or an oxygen atom.

(11) A pharmaceutical comprising, as an active ingredient, the compound according to any of (1) to (10) above.

(12) An interferon inducer comprising, as an active ingredient, the compound according to any of (1) to (10) above.

(13) An antiviral agent comprising, as an active ingredient, the compound according to any of (1) to (10) above.

(14) An anticancer agent comprising, as an active ingredient, the compound according to any of (1) to (10) above.

(15) A type 2 helper T cell selective immune response inhibitor comprising, as an active ingredient, the compound according to any of (1) to (10) above.

(16) An antiallergic agent comprising, as an active ingredient, the compound according to any of (1) to (10) above.

(17) An immune response modulator comprising, as an active ingredient, the compound according to any of (1) to (10) above.

[0008] The compounds according to the present invention are hereafter described in detail.

[0009] In general formula (I), alkyl, alkenyl, or alkynyl represented by R^1 is preferably C_{1-8} alkyl, C_{2-8} alkenyl, or C_{2-8} alkynyl. Further, examples of substituents of alkyl, alkenyl, or alkynyl represented by R^1 include hydroxyl, C_{1-8} alkoxy, aryl, heteroaryl, and a halogen atom (e.g., chlorine, fluorine, bromine, or iodine). Particularly preferable examples of substituted alkyl, alkenyl, or alkynyl represented by R^1 include C_{2-8} alkoxyalkyl, C_{1-8} hydroxyalkyl, aralkyl, and heteroarylalkyl.

[0010] Examples of the aforementioned C_{1-8} alkyl include methyl, ethyl, 1-propyl, 2-propyl, 1-butyl, 2-butyl, 1-pentyl, 2-pentyl, 1-hexyl, 2-hexyl, 1-heptyl, 2-heptyl, 3-heptyl, octyl, 2-methylpropyl, 2-methylbutyl, 3-methylbutyl, 2-methylpentyl, 3-methylpentyl, 4-methylpentyl, methylhexyl, methylheptyl, 1,1-dimethylethyl, 1,1-dimethylpropyl, 2-ethylhexyl,

cyclopentylmethyl, cyclohexylmethyl, cyclopropyl, cyclobutyl, cyclopentyl, methylcyclopentyl, cyclohexyl, methylcyclohexyl, cycloheptyl, and cyclooctyl.

[0011] Examples of the aforementioned C_{2-8} alkenyl include vinyl, allyl, crotyl, 1-propenyl, cyclopentenyl, cyclopentadienyl, and cyclohexenyl.

[0012] Examples of the aforementioned C_{2-8} alkynyl include ethynyl, propynyl, and butynyl.

[0013] Examples of the aforementioned C_{1-8} hydroxyalkyl include 1-hydroxyethyl, 2-hydroxyethyl, 1-hydroxypropyl, 2-hydroxypropyl, 3-hydroxypropyl, 1-hydroxybutyl, 2-hydroxybutyl, 3-hydroxybutyl, and 4-hydroxybutyl.

[0014] Examples of the aforementioned aralkyl include benzyl, 1-phenethyl, 2-phenethyl, phenylpropyl, and phenylbutyl.

[0015] Examples of the aforementioned heteroarylalkyl include 4-pyridylmethyl and 3-pyri dylmethyl.

[0016] Examples of the aforementioned C_{2-8} alkoxyalkyl include methoxymethyl, 2-methoxyethyl, 3-methoxypropyl, 4-methoxybutyl, ethoxymethyl, 2-ethoxyethyl, and 3-ethoxypropyl.

[0017] Each of the aforementioned substituents represented by R^1 may have a substituent such as alkyl, hydroxyl, mercapto, a halogen atom, amino, or alkoxy.

[0018] In general formula (I), examples of aryl or heteroaryl represented by R^1 include phenyl, 1-naphthyl, 2-naphthyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-pyrazinyl, 3-pyrazinyl, 2-pyrimidinyl, 4-pyrimidinyl, 5-pyrimidinyl, 2-furyl, 3-furyl, 2-thienyl, and 3-thienyl. The aforementioned aryl or heteroaryl may or may not have a substituent. Examples of substituents include C_{1-4} alkyl, C_{1-4} alkoxy, hydroxyl, mercapto, C_{1-4} alkylthio, a halogen atom, amino, C_{2-8} dialkylamino, C_{1-4} monoalkylamino, and methylenedioxy. Examples of the aforementioned C_{1-4} alkyl include methyl, ethyl, 1-propyl, 2-propyl, 1-butyl, and 2-butyl. Examples of C_{1-4} alkoxy include methoxy, ethoxy, 1-propoxy, 2-propoxy, 1-butoxy, and 2-butoxy. Examples of the aforementioned C_{2-8} dialkylamino include dimethylamino, diethylamino, dipropylamino, dibutylamino, ethylmethylamino, and methylpropylamino. Examples of the aforementioned C_{1-4} monoalkylamino include methylamino, ethylamino, propylamino, and butylamino. Examples of the aforementioned C_{1-4} alkylthio include methylthio, ethylthio, 1-propylthio, 2-propylthio, 1-butylthio, 2-butylthio, and t-butylthio. Examples of the aforementioned halogen atom include fluorine, chlorine, and bromine.

[0019] Examples of aryl or heteroaryl represented by R^1 having a substituent include 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-ethylphenyl, 3-ethylphenyl, 4-ethylphenyl, 2-propylphenyl, 3-propylphenyl, 4-propylphenyl, 2-isopropylphenyl, 3-isopropylphenyl, 4-isopropylphenyl, 2-butylphenyl, 3-butylphenyl, 4-butylphenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2-ethoxyphenyl, 3-ethoxyphenyl, 4-ethoxyphenyl, 2-propoxyphenyl, 3-propoxyphenyl, 4-propoxyphenyl, 2-isopropoxyphenyl, 3-isopropoxyphenyl, 4-isopropoxyphenyl, 2-butoxyphenyl, 3-butoxyphenyl, 4-butoxyphenyl, 2-methylaminophenyl, 3-methylaminophenyl, 4-methylaminophenyl, 2-ethylaminophenyl, 3-ethylaminophenyl, 4-ethylaminophenyl, 2-propylaminophenyl, 3-propylaminophenyl, 4-propylaminophenyl, 2-isopropylaminophenyl, 3-isopropylaminophenyl, 4-isopropylaminophenyl, 2-butylaminophenyl, 3-butylaminophenyl, 4-butylaminophenyl, 2-dimethylaminophenyl, 3-dimethylaminophenyl, 4-dimethylaminophenyl, 2-diethylaminophenyl, 3-diethylaminophenyl, 4-diethylaminophenyl, 2-dipropylaminophenyl, 3-dipropylaminophenyl, 4-dipropylaminophenyl, 2-dibutylaminophenyl, 3-dibutylaminophenyl, 4-dibutylaminophenyl, 2-ethylmethylaminophenyl, 3-ethylmethylaminophenyl, 4-ethylmethylaminophenyl, 2-methylthiophenyl, 3-methylthiophenyl, 4-methylthiophenyl, 2-ethylthiophenyl, 3-ethylthiophenyl, 4-ethylthiophenyl, 2-propylthiophenyl, 3-propylthiophenyl, 4-propylthiophenyl, 2-isopropylthiophenyl, 3-isopropylthiophenyl, 4-isopropylthiophenyl, 2-butylthiophenyl, 3-butylthiophenyl, 4-butylthiophenyl, 2-methyl-1-naphthyl, 3-methyl-1-naphthyl, 4-methyl-1-naphthyl, 5-methyl-1-naphthyl, 6-methyl-1-naphthyl, 7-methyl-1-naphthyl, 8-methyl-1-naphthyl, 1-methyl-2-naphthyl, 3-methyl-2-naphthyl, 4-methyl-2-naphthyl, 5-methyl-2-naphthyl, 6-methyl-2-naphthyl, 7-methyl-2-naphthyl, 8-methyl-2-naphthyl, 2-methoxy-1-naphthyl, 3-methoxy-1-naphthyl, 4-methoxy-1-naphthyl, 5-methoxy-1-naphthyl, 6-methoxy-1-naphthyl, 7-methoxy-1-naphthyl, 8-methoxy-1-naphthyl, 1-methoxy-2-naphthyl, 3-methoxy-2-naphthyl, 4-methoxy-2-naphthyl, 5-methoxy-2-naphthyl, 6-methoxy-2-naphthyl, 7-methoxy-2-naphthyl, 8-methoxy-2-naphthyl, 2-ethoxy-1-naphthyl, 3-ethoxy-1-naphthyl, 4-ethoxy-1-naphthyl, 5-ethoxy-1-naphthyl, 6-ethoxy-1-naphthyl, 7-ethoxy-1-naphthyl, 8-ethoxy-1-naphthyl, 1-ethoxy-2-naphthyl, 3-ethoxy-2-naphthyl, 4-ethoxy-2-naphthyl, 5-ethoxy-2-naphthyl, 6-ethoxy-2-naphthyl, 7-ethoxy-2-naphthyl, 8-ethoxy-2-naphthyl, 2-hydroxy-1-naphthyl, 3-hydroxy-1-naphthyl, 4-hydroxy-1-naphthyl, 5-hydroxy-1-naphthyl, 6-hydroxy-1-naphthyl, 7-hydroxy-1-naphthyl, 8-hydroxy-1-naphthyl, 1-hydroxy-2-naphthyl, 3-hydroxy-2-naphthyl, 4-hydroxy-2-naphthyl, 5-hydroxy-2-naphthyl, 6-hydroxy-2-naphthyl, 7-hydroxy-2-naphthyl, 8-hydroxy-2-naphthyl, 2-chloro-1-naphthyl, 3-chloro-1-naphthyl, 4-chloro-1-naphthyl, 5-chloro-1-naphthyl, 6-chloro-1-naphthyl, 7-chloro-1-naphthyl, 8-chloro-1-naphthyl, 1-chloro-2-naphthyl, 3-chloro-2-naphthyl, 4-chloro-2-naphthyl, 5-chloro-2-naphthyl, 6-chloro-2-naphthyl, 7-chloro-2-naphthyl, 8-chloro-2-naphthyl, 2-fluoro-1-naphthyl, 3-fluoro-1-naphthyl, 4-fluoro-1-naphthyl, 5-fluoro-1-naphthyl, 6-fluoro-1-naphthyl, 7-fluoro-1-naphthyl, 8-fluoro-1-naphthyl, 1-fluoro-2-naphthyl, 3-fluoro-2-naphthyl, 4-fluoro-2-naphthyl, 5-fluoro-2-naphthyl, 6-fluoro-2-naphthyl, 7-fluoro-2-naphthyl, 8-fluoro-2-naphthyl, 2-amino-1-naphthyl, 3-amino-1-naphthyl, 4-amino-1-naphthyl, 5-amino-1-naphthyl, 6-amino-1-naphthyl, 7-amino-1-naphthyl, 8-amino-1-naphthyl, 1-amino-2-naphthyl, 3-amino-2-naphthyl, 4-amino-2-naphthyl, 5-amino-2-naphthyl, 6-amino-2-naphthyl, 7-amino-2-naphthyl,

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4-methyl-3-furyl, 5-methyl-3-furyl, 3-methoxy-2-furyl, 4-methoxy-2-furyl, 5-methoxy-2-furyl, 2-methoxy-3-furyl, 4-methoxy-3-furyl, 5-methoxy-3-furyl, 3-chloro-2-furyl, 4-chloro-2-furyl, 5-chloro-2-furyl, 2-chloro-3-furyl, 4-chloro-3-furyl, 5-chloro-3-furyl, 3-fluoro-2-furyl, 4-fluoro-2-furyl, 5-fluoro-2-furyl, 2-fluoro-3-furyl, 4-fluoro-3-furyl, 5-fluoro-3-furyl, 3-methyl-2-thienyl, 4-methyl-2-thienyl, 5-methyl-2-thienyl, 2-methyl-3-thienyl, 4-methyl-3-thienyl, 5-methyl-3-thienyl, 3-methoxy-2-thienyl, 4-methoxy-2-thienyl, 5-methoxy-2-thienyl, 2-methoxy-3-thienyl, 4-methoxy-3-thienyl, 5-methoxy-3-thienyl, 3-chloro-2-thienyl, 4-chloro-2-thienyl, 5-chloro-2-thienyl, 2-chloro-3-thienyl, 4-chloro-3-thienyl, 5-chloro-3-thienyl, 3-fluoro-2-thienyl, 4-fluoro-2-thienyl, 5-fluoro-2-thienyl, 2-fluoro-3-thienyl, 4-fluoro-3-thienyl, and 5-fluoro-3-thienyl.

[0020] In general formula (I), examples of substituents represented by R^2 include hydroxyl, mercapto, C_{1-8} acyloxy, and C_{2-8} alkoxycarbonyloxy.

[0021] Examples of the aforementioned C_{1-8} acyloxy include formyloxy, acetyloxy, propionyloxy, butanoyloxy, pentanoyloxy, hexanoyloxy, heptanoyloxy, octanoyloxy, and benzoyloxy.

[0022] Examples of the aforementioned C_{2-8} alkoxycarbonyloxy include methoxycarbonyloxy, ethoxycarbonyloxy, propoxycarbonyloxy, butoxycarbonyloxy, pentyloxycarbonyloxy, hexyloxycarbonyloxy, heptyloxycarbonyloxy, isopropyloxycarbonyloxy, isobutyloxycarbonyloxy, t-butyloxycarbonyloxy, isopentyloxycarbonyloxy, and benzyloxycarbonyloxy.

[0023] In general formula (I), X represents any of NR^3, an oxygen atom, or a sulfur atom, wherein the aforementioned R^3 represents a hydrogen atom or C_{1-3} alkyl, and examples of the alkyl include methyl, ethyl, n-propyl, and isopropyl.

[0024] In general formula (I), examples of 5- or 6-membered monocyclic aromatic hetero rings containing 1 or 2 hetero atoms selected from a nitrogen atom, an oxygen atom, or a sulfur atom represented by Y include thiophene ring, furan ring, pyrrole ring, thiazole ring, isoxazole ring, oxazole ring, pyrazole ring, imidazole ring, pyridine ring, pyrazine ring, pyrimidine ring, and pyridazine ring. Examples of fused bicyclic aromatic hetero rings containing 1 or 2 hetero atoms selected from a nitrogen atom, an oxygen atom, or a sulfur atom include benzothiophene ring, benzofuran ring, indole ring, benzothiazole ring, benzoxazole ring, benzoimidazole ring, quinoline ring, and isoquinoline ring. The aforementioned Y may be unsubstituted or partially substituted by a substituent. Examples of preferable Y include naphthalene ring, thiophene ring, pyridine ring, and pyrazine ring, and these rings may be unsubstituted or partially substituted by a substituent. For example, when Y is a pyridine ring, one to four substituents may substitute at any position on a pyridine ring. When Y is a pyrazine ring, one to three substituents may substitute at any position on a pyrazine ring. When Y is substituted with two or more substituents, they may be the same or different.

[0025] Examples of the substituents for Y include C_{1-4} alkyl, C_{1-4} alkoxy, hydroxyl, mercapto, C_{1-4} alkylthio, a halogen atom, amino, C_{2-8} dialkylamino, C_{1-4} monoalkylamino, 1-pyrrolidinyl, 2-pyrrolidinyl, 3-pyrrolidinyl, piperidino, morpholino, and 3-morpholinyl. Alkyl in the aforementioned C_{1-4} alkyl and C_{1-4} alkoxy, further in the aforementioned C_{2-8} dialkylamino and C_{1-4} monoalkylamino is the same as that in the aforementioned case of R^1. Examples of the aforementioned C_{1-4} alkylthio include methylthio, ethylthio, 1-propylthio, 2-propylthio, 1-butylthio, 2-butylthio, and t-butylthio. Examples of the aforementioned halogen atom include fluorine, chlorine, and bromine.

[0026] Examples of Y having a substituent include 2-methyl-1-naphthyl, 3-methyl-1-naphthyl, 4-methyl-1-naphthyl, 5-methyl-1-naphthyl, 6-methyl-1-naphthyl, 7-methyl-1-naphthyl, 8-methyl-1-naphthyl, 1-methyl-2-naphthyl, 3-methyl-2-naphthyl, 4-methyl-2-naphthyl, 5-methyl-2-naphthyl, 6-methyl-2-naphthyl, 7-methyl-2-naphthyl, 8-methyl-2-naphthyl, 2-methoxy-1-naphthyl, 3-methoxy-1-naphthyl, 4-methoxy-1-naphthyl, 5-methoxy-1-naphthyl, 6-methoxy-1-naphthyl, 7-methoxy-1-naphthyl, 8-methoxy-1-naphthyl, 1-methoxy-2-naphthyl, 3-methoxy-2-naphthyl, 4-methoxy-2-naphthyl, 5-methoxy-2-naphthyl, 6-methoxy-2-naphthyl, 7-methoxy-2-naphthyl, 8-methoxy-2-naphthyl, 2-ethoxy-1-naphthyl, 3-ethoxy-1-naphthyl, 4-ethoxy-1-naphthyl, 5-ethoxy-1-naphthyl, 6-ethoxy-1-naphthyl, 7-ethoxy-1-naphthyl, 8-ethoxy-1-naphthyl, 1-ethoxy-2-naphthyl, 3-ethoxy-2-naphthyl, 4-ethoxy-2-naphthyl, 5-ethoxy-2-naphthyl, 6-ethoxy-2-naphthyl, 7-ethoxy-2-naphthyl, 8-ethoxy-2-naphthyl, 2-hydroxy-1-naphthyl, 3-hydroxy-1-naphthyl, 4-hydroxy-1-naphthyl, 5-hydroxy-1-naphthyl, 6-hydroxy-1-naphthyl, 7-hydroxy-1-naphthyl, 8-hydroxy-1-naphthyl, 1-hydroxy-2-naphthyl, 3-hydroxy-2-naphthyl, 4-hydroxy-2-naphthyl, 5-hydroxy-2-naphthyl, 6-hydroxy-2-naphthyl, 7-hydroxy-2-naphthyl, 8-hydroxy-2-naphthyl, 2-chloro-1-naphthyl, 3-chloro-1-naphthyl, 4-chloro-1-naphthyl, 5-chloro-1-naphthyl, 6-chloro-1-naphthyl, 7-chloro-1-naphthyl, 8-chloro-1-naphthyl, 1-chloro-2-naphthyl, 3-chloro-2-naphthyl, 4-chloro-2-naphthyl, 5-chloro-2-naphthyl, 6-chloro-2-naphthyl, 7-chloro-2-naphthyl, 8-chloro-2-naphthyl, 2-fluoro-1-naphthyl, 3-fluoro-1-naphthyl, 4-fluoro-1-naphthyl, 5-fluoro-1-naphthyl, 6-fluoro-1-naphthyl, 7-fluoro-1-naphthyl, 8-fluoro-1-naphthyl, 1-fluoro-2-naphthyl, 3-fluoro-2-naphthyl, 4-fluoro-2-naphthyl, 5-fluoro-2-naphthyl, 6-fluoro-2-naphthyl, 7-fluoro-2-naphthyl, 8-fluoro-2-naphthyl, 2-amino-1-naphthyl, 3-amino-1-naphthyl, 4-amino-1-naphthyl, 5-amino-1-naphthyl, 6-amino-1-naphthyl, 7-amino-1-naphthyl, 8-amino-1-naphthyl, 1-amino-2-naphthyl, 3-amino-2-naphthyl, 4-amino-2-naphthyl, 5-amino-2-naphthyl, 6-amino-2-naphthyl, 7-amino-2-naphthyl, 8-amino-2-naphthyl, 2-methylamino-1-naphthyl, 3-methylamino-1-naphthyl, 4-methylamino-1-naphthyl, 5-methylamino-1-naphthyl, 6-methylamino-1-naphthyl, 7-methylamino-1-naphthyl, 8-methylamino-1-naphthyl, 1-methylamino-2-naphthyl, 3-methylamino-2-naphthyl, 4-methylamino-2-naphthyl, 5-methylamino-2-naphthyl, 6-methylamino-2-naphthyl, 7-methylamino-2-naphthyl, 8-methylamino-2-naphthyl, 2-dimethylamino-1-naphthyl, 3-dimethylamino-1-naphthyl, 4-dimethylamino-1-naphthyl, 5-dimethylamino-1-naphthyl, 6-dimethylamino-1-naphthyl, 7-dimethylamino-1-naphthyl, 8-dimethylamino-1-naphthyl, 1-dimethylamino-2-naphthyl, 3-dimethylamino-2-naphthyl, 4-dimethylamino-2-naphthyl, 5-dimethylamino-2-naphthyl, 6-dimethylamino-2-naphthyl, 7-dimethylamino-2-naphthyl, 8-dimethylamino-2-naphthyl, 3-methyl-2-thienyl, 4-methyl-2-thienyl, 5-methyl-2-thienyl, 2-methyl-3-thienyl, 4-methyl-3-thienyl, 5-methyl-3-thienyl, 3-methoxy-2-thienyl, 4-methoxy-2-thienyl, 5-methoxy-2-thienyl, 2-methoxy-3-thienyl, 4-methoxy-3-thienyl, 5-methoxy-3-thienyl, 3-chloro-2-thienyl, 4-chloro-2-thienyl, 5-chloro-2-thienyl, 2-chloro-3-thienyl, 4-chloro-3-thienyl, 5-chloro-3-thienyl, 3-fluoro-2-thienyl, 4-fluoro-2-thienyl, 5-fluoro-2-thienyl, 2-fluoro-3-thienyl, 4-fluoro-3-thienyl, 5-fluoro-3-thienyl, 3-methyl-2-furyl, 4-methyl-2-furyl, 5-methyl-2-furyl, 2-methyl-3-furyl, 4-methyl-3-furyl, 5-methyl-3-furyl, 3-methoxy-2-furyl, 4-methoxy-2-furyl, 5-methoxy-2-furyl, 2-methoxy-3-furyl, 4-methoxy-3-furyl, 5-methoxy-3-furyl, 3-chloro-2-furyl, 4-chloro-2-furyl, 5-chloro-2-furyl, 2-chloro-3-furyl, 4-chloro-3-furyl, 5-chloro-3-furyl, 3-fluoro-2-furyl, 4-fluoro-2-furyl, 5-fluoro-2-furyl, 2-fluoro-3-furyl, 4-fluoro-3-furyl, 5-fluoro-3-furyl, 3-methyl-2-pyrrolyl, 4-methyl-2-pyrrolyl, 5-methyl-2-pyrrolyl, 2-methyl-3-pyrrolyl, 4-methyl-3-pyrrolyl, 5-methyl-3-pyrrolyl, 3-methoxy-2-pyrrolyl, 4-methoxy-2-pyrrolyl, 5-methoxy-2-pyrrolyl, 2-methoxy-3-pyrrolyl, 4-methoxy-3-pyrrolyl, 5-methoxy-3-pyrrolyl, 3-chloro-2-pyrrolyl, 4-chloro-2-pyrrolyl, 5-chloro-2-pyrrolyl, 2-chloro-3-pyrrolyl, 4-chloro-3-pyrrolyl, 5-chloro-3-pyrrolyl, 3-fluoro-2-pyrrolyl, 4-fluoro-2-pyrrolyl, 5-fluoro-2-pyrrolyl, 2-fluoro-3-pyrrolyl, 4-fluoro-3-pyrrolyl, 5-fluoro-3-pyrrolyl, 1-methyl-2-imidazolyl, 4-methyl-2-imidazolyl, 1-methyl-4-imidazolyl, 2-methyl-4-imidazolyl, 5-methyl-4-imidazolyl, 1-methyl-5-imidazolyl, 4-methoxy-2-imida-

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6-dimethylamino-2-pyridyl, 2-dimethylamino-4-pyridyl, 3-dimethylamino-4-pyridyl, 5-dimethylamino-4-pyridyl, 6-dimethylamino-4-pyridyl, 2-(1-pyrrolidinyl)-3-pyridyl, 4-(1-pyrrolidinyl)-3-pyridyl, 5-(1-pyrrolidinyl)-3-pyridyl, 6-(1-pyrrolidinyl)-3-pyridyl, 3-(1-pyrrolidinyl)-2-pyridyl, 4-(1-pyrrolidinyl)-2-pyridyl, 5-(1-pyrrolidinyl)-2-pyridyl, 6-(1-pyrrolidinyl)-2-pyridyl, 2-(1-pyrrolidinyl)-4-pyridyl, 3-(1-pyrrolidinyl)-4-pyridyl, 5-(1-pyrrolidinyl)-4-pyridyl, 6-(1-pyrrolidinyl)-4-pyridyl, 2-piperidino-3-pyridyl, 4-piperidino-3-pyridyl, 5-piperidino-3-pyridyl, 6-piperidino-3-pyridyl, 3-piperidino-2-pyridyl, 4-piperidino-2-pyridyl, 5-piperidino-2-pyridyl, 6-piperidino-2-pyridyl, 2-piperidino-4-pyridyl, 3-piperidino-4-pyridyl, 5-piperidino-4-pyridyl, 6-piperidino-4-pyridyl, 2-morpholino-3-pyridyl, 4-morpholino-3-pyridyl, 5-morpholino-3-pyridyl, 6-morpholino-3-pyridyl, 3-morpholino-2-pyridyl, 4-morpholino-2-pyridyl, 5-morpholino-2-pyridyl, 6-morpholino-2-pyridyl, 2-morpholino-4-pyridyl, 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5-chloro-6-methoxy-3-pyridyl, 5-chloro-6-ethoxy-3-pyridyl, 2,5,6-trimethyl-3-pyridyl, 2-pyrazinyl, 5-methyl-2-pyrazinyl, 6-methyl-2-pyrazinyl, 5-methoxy-2-pyrazinyl, 6-methoxy-2-pyrazinyl, 5-ethoxy-2-pyrazinyl, 6-ethoxy-2-pyrazinyl, 5-chloro-2-pyrazinyl, 6-chloro-2-pyrazinyl, 3-methyl-2-benzothienyl, 4-methyl-2-benzothienyl, 5-methyl-2-benzothienyl, 6-methyl-2-benzothienyl, 7-methyl-2-benzothienyl, 2-methyl-3-benzothienyl, 4-methyl-3-benzothienyl, 5-methyl-3-benzothienyl, 6-methyl-3-benzothienyl, 7-methyl-3-benzothienyl, 2-methyl-5-benzothienyl, 3-methyl-5-benzothienyl, 4-methyl-5-benzothienyl, 6-methyl-5-benzothienyl, 7-methyl-5-benzothienyl, 3-methoxy-2-benzothienyl, 4-methoxy-2-benzothienyl, 5-methoxy-2-benzothienyl, 6-methoxy-2-benzothienyl, 7-methoxy-2-benzothienyl, 2-methoxy-3-benzothienyl, 4-methoxy-3-benzothienyl, 5-methoxy-3-benzothienyl, 6-methoxy-3-benzothienyl, 7-methoxy-3-benzothienyl, 2-methoxy-5-benzothienyl, 3-methoxy-5-benzothienyl, 4-methoxy-5-benzothienyl, 6-methoxy-5-benzothienyl, 7-methoxy-5-benzothienyl, 3-chloro-2-benzothienyl, 4-chloro-2-benzothienyl, 5-chloro-2-benzothienyl, 6-chloro-2-benzothienyl, 7-chloro-2-benzothienyl, 2-chloro-3-benzothienyl, 4-chloro-3-benzothienyl, 5-chloro-3-benzothienyl, 6-chloro-3-benzothienyl, 7-chloro-3-benzothienyl, 2-chloro-5-benzothienyl, 3-chloro-5-benzothienyl, 4-chloro-5-benzothienyl, 6-chloro-5-benzothienyl, 7-chloro-5-benzothienyl, 3-fluoro-2-benzothienyl, 4-fluoro-2-benzothienyl, 5-fluoro-2-benzothienyl, 6-fluoro-2-benzothienyl, 7-fluoro-2-benzothienyl, 2-fluoro-3-benzothienyl, 4-fluoro-3-benzothienyl, 5-fluoro-3-benzothienyl, 6-fluoro-3-benzothienyl, 7-fluoro-3-benzothienyl, 2-fluoro-5-benzothienyl, 3-fluoro-5-benzothienyl, 4-fluoro-5-benzothienyl, 6-fluoro-5-benzothienyl, 7-fluoro-5-benzothienyl, 3-methyl-2-benzo-

furyl, 4-methyl-2-benzofuryl, 5-methyl-2-benzofuryl, 6-methyl-2-benzofuryl, 7-methyl-2-benzofuryl, 2-methyl-3-benzofuryl, 4-methyl-3-benzofuryl, 5-methyl-3-benzofuryl, 6-methyl-3-benzofuryl, 7-methyl-3-benzofuryl, 2-methyl-5-benzofuryl, 3-methyl-5-benzofuryl, 4-methyl-5-benzofuryl, 6-methyl-5-benzofuryl, 7-methyl-5-benzofuryl, 3-methoxy-2-benzofuryl, 4-methoxy-2-benzofuryl, 5-methoxy-2-benzofuryl, 6-methoxy-2-benzofuryl, 7-methoxy-2-benzofuryl, 2-methoxy-3-benzofuryl, 4-methoxy-3-benzofuryl, 5-methoxy-3-benzofuryl, 6-methoxy-3-benzofuryl, 7-methoxy-3-benzofuryl, 2-methoxy-5-benzofuryl, 3-methoxy-5-benzofuryl, 4-methoxy-5-benzofuryl, 6-methoxy-5-benzofuryl, 7-methoxy-5-benzofuryl, 3-chloro-2-benzofuryl, 4-chloro-2-benzofuryl, 5-chloro-2-benzofuryl, 6-chloro-2-benzofuryl, 7-chloro-2-benzofuryl, 2-chloro-3-benzofuryl, 4-chloro-3-benzofuryl, 5-chloro-3-benzofuryl, 6-chloro-3-benzofuryl, 7-chloro-3-benzofuryl, 2-chloro-5-benzofuryl, 3-chloro-5-benzofuryl, 4-chloro-5-benzofuryl, 6-chloro-5-benzofuryl, 7-chloro-5-benzofuryl, 3-fluoro-2-benzofuryl, 4-fluoro-2-benzofuryl, 5-fluoro-2-benzofuryl, 6-fluoro-2-benzofuryl, 7-fluoro-2-benzofuryl, 2-fluoro-3-benzofuryl, 4-fluoro-3-benzofuryl, 5-fluoro-3-benzofuryl, 6-fluoro-3-benzofuryl, 7-fluoro-3-benzofuryl, 2-fluoro-5-benzofuryl, 3-fluoro-5-benzofuryl, 4-fluoro-5-benzofuryl, 6-fluoro-5-benzofuryl, 7-fluoro-5-benzofuryl, 1-methyl-2-indolyl, 3-methyl-2-indolyl, 4-methyl-2-indolyl, 5-methyl-2-indolyl, 6-methyl-2-indolyl, 7-methyl-2-indolyl, 1-methyl-3-indolyl, 2-methyl-3-indolyl, 4-methyl-3-indolyl, 5-methyl-3-indolyl, 6-methyl-3-indolyl, 7-methyl-3-indolyl, 1-methyl-5-indolyl, 2-methyl-5-indolyl, 3-methyl-5-indolyl, 4-methyl-5-indolyl, 6-methyl-5-indolyl, 7-methyl-5-indolyl, 3-methoxy-2-indolyl, 4-methoxy-2-indolyl, 5-methoxy-2-indolyl, 6-methoxy-2-indolyl, 7-methoxy-2-indolyl, 2-methoxy-3-indolyl, 4-methoxy-3-indolyl, 5-methoxy-3-indolyl, 6-methoxy-3-indolyl, 7-methoxy-3-indolyl, 2-methoxy-5-indolyl, 3-methoxy-5-indolyl, 4-methoxy-5-indolyl, 6-methoxy-5-indolyl, 7-methoxy-5-indolyl, 3-chloro-2-indolyl, 4-chloro-2-indolyl, 5-chloro-2-indolyl, 6-chloro-2-indolyl, 7-chloro-2-indolyl, 2-chloro-3-indolyl, 4-chloro-3-indolyl, 5-chloro-3-indolyl, 6-chloro-3-indolyl, 7-chloro-3-indolyl, 2-chloro-5-indolyl, 3-chloro-5-indolyl, 4-chloro-5-indolyl, 6-chloro-5-indolyl, 7-chloro-5-indolyl, 3-fluoro-2-indolyl, 4-fluoro-2-indolyl, 5-fluoro-2-indolyl, 6-fluoro-2-indolyl, 7-fluoro-2-indolyl, 2-fluoro-3-indolyl, 4-fluoro-3-indolyl, 5-fluoro-3-indolyl, 6-fluoro-3-indolyl, 7-fluoro-3-indolyl, 2-fluoro-5-indolyl, 3-fluoro-5-indolyl, 4-fluoro-5-indolyl, 6-fluoro-5-indolyl, 7-fluoro-5-indolyl, 3-methyl-2-quinolyl, 4-methyl-2-quinolyl, 5-methyl-2-quinolyl, 6-methyl-2-quinolyl, 7-methyl-2-quinolyl, 8-methyl-2-quinolyl, 2-methyl-4-quinolyl, 3-methyl-4-quinolyl, 5-methyl-4-quinolyl, 6-methyl-4-quinolyl, 7-methyl-4-quinolyl, 8-methyl-4-quinolyl, 2-methyl-6-quinolyl, 3-methyl-6-quinolyl, 4-methyl-6-quinolyl, 5-methyl-6-quinolyl, 7-methyl-6-quinolyl, 8-methyl-6-quinolyl, 3-methoxy-2-quinolyl, 4-methoxy-2-quinolyl, 5-methoxy-2-quinolyl, 6-methoxy-2-quinolyl, 7-methoxy-2-quinolyl, 8-methoxy-2-quinolyl, 2-methoxy-4-quinolyl, 3-methoxy-4-quinolyl, 5-methoxy-4-quinolyl, 6-methoxy-4-quinolyl, 7-methoxy-4-quinolyl, 8-methoxy-4-quinolyl, 2-methoxy-6-quinolyl, 3-methoxy-6-quinolyl, 4-methoxy-6-quinolyl, 5-methoxy-6-quinolyl, 7-methoxy-6-quinolyl, 8-methoxy-6-quinolyl, 3-chloro-2-quinolyl, 4-chloro-2-quinolyl, 5-chloro-2-quinolyl, 6-chloro-2-quinolyl, 7-chloro-2-quinolyl, 8-chloro-2-quinolyl, 2-chloro-4-quinolyl, 3-chloro-4-quinolyl, 5-chloro-4-quinolyl, 6-chloro-4-quinolyl, 7-chloro-4-quinolyl, 8-chloro-4-quinolyl, 2-chloro-6-quinolyl, 3-chloro-6-quinolyl, 4-chloro-6-quinolyl, 5-chloro-6-quinolyl, 7-chloro-6-quinolyl, 8-chloro-6-quinolyl, 3-fluoro-2-quinolyl, 4-fluoro-2-quinolyl, 5-fluoro-2-quinolyl, 6-fluoro-2-quinolyl, 7-fluoro-2-quinolyl, 8-fluoro-2-quinolyl, 2-fluoro-4-quinolyl, 3-fluoro-4-quinolyl, 5-fluoro-4-quinolyl, 6-fluoro-4-quinolyl, 7-fluoro-4-quinolyl, 8-fluoro-4-quinolyl, 2-fluoro-6-quinolyl, 3-fluoro-6-quinolyl, 4-fluoro-6-quinolyl, 5-fluoro-6-quinolyl, 7-fluoro-6-quinolyl, and 8-fluoro-6-quinolyl.

[0027] In general formula (I), examples of further preferable X include NH and an oxygen atom, with NH being particularly preferable.

[0028] In general formula (I), examples of further preferable R^1 include C_{1-6} alkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl. Specific examples thereof include methyl, ethyl, propyl, isopropyl, butyl, 2-butyl, pentyl, 2-pentyl, hexyl, 2-hexyl, vinyl, propenyl, butenyl, butynyl, and pentenyl. Among them, C_{3-5} alkyl, C_{3-5} alkenyl, and C_{3-5} alkynyl, more specifically, propyl, isopropyl, butyl, 2-butyl, pentyl, 2-pentyl, propenyl, butenyl, butynyl, and pentenyl are further preferable, with propyl, butyl, and pentyl being particularly preferable.

[0029] In general formula (I), examples of further preferable R^2 include hydroxyl, acetyloxy, propionyloxy, methoxycarbonyloxy, ethoxycarbonyloxy, propoxycarbonyloxy, and butoxycarbonyloxy, with hydroxyl, methoxycarbonyloxy, and ethoxycarbonyloxy being particularly preferable.

[0030] In general formula (I), examples of further preferable Y include a substituted or unsubstituted pyridine ring (e.g., 2-pyridyl, 3-pyridyl, and 4-pyridyl) and a pyrazine ring (e.g., 2-pyrazinyl and 3-pyrazinyl), with 3-pyridyl being particularly preferable. Examples of further preferable Y having a substituent include 2-methyl-3-pyridyl, 6-methyl-3-pyridyl, 2-ethyl-3-pyridyl, 6-ethyl-3-pyridyl, 2-methoxy-3-pyridyl, 6-methoxy-3-pyridyl, 2-ethoxy-3-pyridyl, 6-ethoxy-3-pyridyl, 2-chloro-3-pyridyl, 6-chloro-3-pyridyl, 6-dimethylamino-3-pyridyl, 6-(1-pyrrolidinyl)-3-pyridyl, 6-piperidino-3-pyridyl, 6-morpholino-3-pyridyl, 6-methylthio-3-pyridyl, 5,6-dimethyl-3-pyridyl, 5,6-dimethoxy-3-pyridyl, 2,6-dichloro-3-pyridyl, 5,6-dichloro-3-pyridyl, and 5-chloro-6-methoxy-3-pyridyl. Among them, 3-pyridyl, 6-methyl-3-pyridyl, 6-methoxy-3-pyridyl, 6-ethoxy-3-pyridyl, 6-chloro-3-pyridyl, 6-(1-pyrrolidinyl)-3-pyridyl, 6-morpholino-3-pyridyl, 2-methyl-3-pyridyl, 2-methoxy-3-pyridyl, and 2-chloro-3-pyridyl are particularly preferable.

[0031] Specific examples of the compounds in the scope of the present invention include the following.

Table 1

X	R^1	R^2	Y
NH	propyl	OH	2-pyridyl
NH	propyl	OH	3-pyridyl
NH	propyl	OH	4-pyridyl
NH	propyl	OH	2-methyl-3-pyridyl
NH	propyl	OH	4-methyl-3-pyridyl
NH	propyl	OH	5-methyl-3-pyridyl
NH	propyl	OH	6-methyl-3-pyridyl
NH	propyl	OH	2-ethyl-3-pyridyl
NH	propyl	OH	4-ethyl-3-pyridyl
NH	propyl	OH	5-ethyl-3-pyridyl
NH	propyl	OH	6-ethyl-3-pyridyl
NH	propyl	OH	2-methoxy-3-pyridyl
NH	propyl	OH	4-methoxy-3-pyridyl
NH	propyl	OH	5-methoxy-3-pyridyl
NH	propyl	OH	6-methoxy-3-pyridyl
NH	propyl	OH	2-ethoxy-3-pyridyl
NH	propyl	OH	4-ethoxy-3-pyridyl
NH	propyl	OH	5-ethoxy-3-pyridyl
NH	propyl	OH	6-ethoxy-3-pyridyl
NH	propyl	OH	2-chloro-3-pyridyl
NH	propyl	OH	4-chloro-3-pyridyl
NH	propyl	OH	5-chloro-3-pyridyl
NH	propyl	OH	6-chloro-3-pyridyl
NH	propyl	OH	2-fluoro-3-pyridyl
NH	propyl	OH	4-fluoro-3-pyridyl
NH	propyl	OH	5-fluoro-3-pyridyl
NH	propyl	OH	6-fluoro-3-pyridyl
NH	propyl	OH	2-dimethylamino-3-pyridyl
NH	propyl	OH	4-dimethylamino-3-pyridyl
NH	propyl	OH	5-dimethylamino-8-pyridyl
NH	propyl	OH	6-dimethylamino-3-pyridyl
NH	propyl	OH	2-(1-pyrrolidinyl)-3-pyridyl
NH	propyl	OH	3-(1-pyrrolidinyl)-3-pyridyl
NH	propyl	OH	5-(1-pyrrolidinyl)-3-pyridyl
NH	propyl	OH	6-(1-pyrrolidinyl)-3-pyridyl
NH	propyl	OH	2-piperidino-3-pyridyl
NH	propyl	OH	4-piperidino-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	propyl	OH	5-piperidino-3-pyridyl
NH	propyl	OH	6-piperidino-3-pyridyl
NH	propyl	OH	2-morpholino-3-pyridyl
NH	propyl	OH	4-morpholino-3-pyridyl
NH	propyl	OH	5-morpholino-3-pyridyl
NH	propyl	OH	6-morpholino-3-pyridyl
NH	propyl	OH	2-hydroxy-3-pyridyl
NH	propyl	OH	4-hydroxy-3-pyridyl
NH	propyl	OH	5-hydroxy-3-pyridyl
NH	propyl	OH	6-hydroxy-3-pyridyl
NH	propyl	OH	2-mercapto-3-pyridyl
NH	propyl	OH	4-mercapto-3-pyridyl
NH	propyl	OH	5-mercapto-3-pyridyl
NH	propyl	OH	6-mercapto-3-pyridyl
NH	propyl	OH	2-methylthio-3-pyridyl
NH	propyl	OH	4-methylthio-3-pyridyl
NH	propyl	OH	5-methylthio-3-pyridyl
NH	propyl	OH	6-methylthio-3-pyridyl
NH	propyl	OH	2,6-dimethyl-3-pyridyl
NH	propyl	OH	5,6-dimethyl-3-pyridyl
NH	propyl	OH	2,6-diethyl-3-pyridyl
NH	propyl	OH	5,6-diethyl-3-pyridyl
NH	propyl	OH	2,6-dimethoxy-3-pyridyl
NH	propyl	OH	5,6-dimethoxy-3-pyridyl
NH	propyl	OH	2,6-diethoxy-3-pyridyl
NH	propyl	OH	5,6-diethoxy-3-pyridyl
NH	propyl	OH	2,6-dichloro-3-pyridyl
NH	propyl	OH	5,6-dichloro-3-pyridyl
NH	propyl	OH	5-chloro-6-methoxy-3-pyridyl
NH	propyl	OH	5-chloro-6-ethoxy-3-pyridyl
NH	propyl	OH	2-chloro-6-methyl-3-pyridyl
NH	propyl	OH	6-chloro-2-methyl-3-pyridyl
NH	propyl	OH	2-methyl-4-pyridyl
NH	propyl	OH	2-ethyl-4-pyridyl
NH	propyl	OH	2-methoxy-4-pyridyl
NH	propyl	OH	2-ethoxy-4-pyridyl
NH	propyl	OH	2-chloro-4-pyridyl
NH	propyl	OH	2-dimethylamino-4-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	propyl	OH	2-(1-pyrrolidinyl)-4-pyridyl
NH	propyl	OH	2-piperidino-4-pyridyl
NH	propyl	OH	2-morpholino-4-pyridyl
NH	propyl	OH	2-methylthio-4-pyridyl
NH	propyl	OH	2-pyrazinyl
NH	propyl	OH	5-methyl-2-pyrazinyl
NH	propyl	OH	5-ethyl-2-pyrazinyl
NH	propyl	OH	5-methoxy-2-pyrazinyl
NH	propyl	OH	5-ethoxy-2-pyrazinyl
NH	propyl	OH	5-chloro-2-pyrazinyl
NH	propyl	OH	6-methyl-2-pyrazinyl
NH	propyl	OH	6-methoxy-2-pyrazinyl
NH	propyl	OH	6-chloro-2-pyrazinyl
NH	propyl	OCOOMe	2-pyridyl
NH	propyl	OCOOMe	3-pyridyl
NH	propyl	OCOOMe	4-pyridyl
NH	propyl	OCOOMe	2-methyl-3-pyridyl
NH	propyl	OCOOMe	4-methyl-3-pyridyl
NH	propyl	OCOOMe	5-methyl-3-pyridyl
NH	propyl	OCOOMe	6-methyl-3-pyridyl
NH	propyl	OCOOMe	2-ethyl-3-pyridyl
NH	propyl	OCOOMe	4-ethyl-3-pyridyl
NH	propyl	OCOOMe	5-ethyl-3-pyridyl
NH	propyl	OCOOMe	6-ethyl-3-pyridyl
NH	propyl	OCOOMe	2-methoxy-3-pyridyl
NH	propyl	OCOOMe	4-methoxy-3-pyridyl
NH	propyl	OCOOMe	5-methoxy-3-pyridyl
NH	propyl	OCOOMe	6-methoxy-3-pyridyl
NH	propyl	OCOOMe	2-ethoxy-3-pyridyl
NH	propyl	OCOOMe	4-ethoxy-3-pyridyl
NH	propyl	OCOOMe	5-ethoxy-3-pyridyl
NH	prupyl	OCOOMe	6-ethoxy-3-pyridyl
NH	propyl	OCOOMe	2-chloro-3-pyridyl
NH	propyl	OCOOMe	4-chloro-3-pyridyl
NH	propyl	OCOOMe	5-chloro-3-pyridyl
NH	propyl	OCOOMe	6-chloro-3-pyridyl
NH	propyl	OCOOMe	2-fluoro-3-pyridyl
NH	propyl	OCOOMe	4-fluoro-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	propyl	OCOOMe	5-fluoro-3-pyridyl
NH	propyl	OCOOMe	6-fluoro-3-pyridyl
NH	propyl	OCOOMe	2-dimethylamino-3-pyridyl
NH	propyl	OCOOMe	4-dimethylamino-3-pyridyl
NH	propyl	OCOOMe	5-dimethylamino-3-pyridyl
NH	propyl	OCOOMe	6-dimethylamino-3-pyridyl
NH	propyl	OCOOMe	2-(1-pyrrolidinyl)-3-pyridyl
NH	propyl	OCOOMe	3-(1-pyrrolidinyl)-3-pyridyl
NH	propyl	OCOOMe	5-(1-pyrrolidinyl)-3-pyridyl
NH	propyl	OCOOMe	6-(1-pyrrolidinyl)-3-pyridyl
NH	propyl	OCOOMe	2-piperidino-3-pyridyl
NH	propyl	OCOOMe	4-piperidino-3-pyridyl
NH	propyl	OCOOMe	5-piperidino-3-pyridyl
NH	propyl	OCOOMe	6-piperidino-3-pyridyl
NH	propyl	OCOOMe	2-morpholino-3-pyridyl
NH	propyl	OCOOMe	4-morpholino-3-pyridyl
NH	propyl	OCOOMe	5-morpholino-3-pyridyl
NH	propyl	OCOOMe	6-morpholino-3-pyridyl
NH	propyl	OCOOMe	2-hydroxy-3-pyridyl
NH	propyl	OCOOMe	4-hydroxy-3-pyridyl
NH	propyl	OCOOMe	5-hydroxy-3-pyridyl
NH	propyl	OCOOMe	6-hydroxy-3-pyridyl
NH	propyl	OCOOMe	2-mercapto-3-pyridyl
NH	propyl	OCOOMe	4-mercapto-3-pyridyl
NH	propyl	OCOOMe	5-mercapto-3-pyridyl
NH	propyl	OCOOMe	6-mercapto-3-pyridyl
NH	propyl	OCOOMe	2-methylthio-3-pyridyl
NH	propyl	OCOOMe	4-methylthio-3-pyridyl
NH	propyl	OCOOMe	5-methylthio-3-pyridyl
NH	propyl	OCOOMe	6-methylthio-3-pyridyl
NH	propyl	OCOOMe	2,6-dimethyl-3-pyridyl
NH	propyl	OCOOMe	5,6-dimethyl-3-pyridyl
NH	propyl	OCOOMe	2,6-diethyl-3-pyridyl
NH	propyl	OCOOMe	5,6-diethyl-3-pyridyl
NH	propyl	OCOOMe	2,6-dimethoxy-3-pyridyl
NH	propyl	OCOOMe	5,6-dimethoxy-3-pyridyl
NH	propyl	OCOOMe	2,6-diethoxy-3-pyridyl
NH	propyl	OCOOMe	5,6-diethoxy-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	propyl	OCOOMe	2,6-dichloro-3-pyridyl
NH	propyl	OCOOMe	5,6-dichloro-3-pyridyl
NH	propyl	OCOOMe	5-chloro-6-methoxy-3-pyridyl
NH	propyl	OCOOMe	5-chloro-6-ethoxy-3-pyridyl
NH	propyl	OCOOMe	2-chloro-6-methyl-3-pyridyl
NH	propyl	OCOOMe	6-chloro-2-methyl-3-pyridyl
NH	propyl	OCOOMe	2-methyl-4-pyridyl
NH	propyl	OCOOMe	2-ethyl-4-pyridyl
NH	propyl	OCOOMe	2-methoxy-4-pyridyl
NH	propyl	OCOOMe	2-ethoxy-4-pyridyl
NH	propyl	OCOOMe	2-chloro-4-pyridyl
NH	propyl	OCOOMe	2-dimethylamino-4-pyridyl
NH	propyl	OCOOMe	2-(1-pyrrolidinyl)-4-pyridyl
NH	propyl	OCOOMe	2-piperidino-4-pyridyl
NH	propyl	OCOOMe	2-morpholino-4-pyridyl
NH	propyl	OCOOMe	2-methylthio-4-pyridyl
NH	propyl	OCOOMe	2-pyrazinyl
NH	propyl	OCOOMe	5-methyl-2-pyrazinyl
NH	propyl	OCOOMe	5-ethyl-2-pyrazinyl
NH	propyl	OCOOMe	5-methoxy-2-pyrazinyl
NH	propyl	OCOOMe	5-ethoxy-2-pyrazinyl
NH	propyl	OCOOMe	5-chloro-2-pyrazinyl
NH	propyl	OCOOMe	6-methyl-2-pyrazinyl
NH	propyl	OCOOMe	6-methoxy-2-pyrazinyl
NH	propyl	OCOOMe	6-chloro-2-pyrazinyl
NH	propyl	OCOOEt	2-pyridyl
NH	propyl	OCOOEt	3-pyridyl
NH	propyl	OCOOEt	4-pyridyl
NH	propyl	OCOOEt	2-methyl-3-pyridyl
NH	propyl	OCOOEt	4-methyl-3-pyridyl
NH	propyl	OCOOEt	5-methyl-3-pyridyl
NH	propyl	OCOOEt	6-methyl-3-pyridyl
NH	propyl	OCOOEt	2-ethyl-3-pyridyl
NH	propyl	OCOOEt	4-ethyl-3-pyridyl
NH	propyl	OCOOEt	5-ethyl-3-pyridyl
NH	propyl	OCOOEt	6-ethyl-3-pyridyl
NH	propyl	OCOOEt	2-methoxy-3-pyridyl
NH	propyl	OCOOEt	4-methoxy-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	propyl	OCOOEt	5-methoxy-3-pyridyl
NH	propyl	OCOOEt	6-methoxy-3-pyridyl
NH	propyl	OCOOEt	2-ethoxy-3-pyridyl
NH	propyl	OCOOEt	4-ethoxy-3-pyridyl
NH	propyl	OCOOEt	5-ethoxy-3-pyridyl
NH	propyl	OCOOEt	6-ethoxy-3-pyridyl
NH	propyl	OCOOEt	2-chloro-3-pyridyl
NH	propyl	OCOOEt	4-chloro-3-pyridyl
NH	propyl	OCOOEt	5-chloro-3-pyridyl
NH	propyl	OCOOEt	6-chloro-3-pyridyl
NH	propyl	OCOOEt	2-fluoro-3-pyridyl
NH	propyl	OCOOEt	4-fluoro-3-pyridyl
NH	propyl	OCOOEt	5-fluoro-3-pyridyl
NH	propyl	OCOOEt	6-fluoro-3-pyridyl
NH	propyl	OCOOEt	2-dimethylamino-3-pyridyl
NH	propyl	OCOOEt	4-dimethylamino-3-pyridyl
NH	propyl	OCOOEt	5-dimethylamino-3-pyridyl
NH	propyl	OCOOEt	6-dimethylamino-3-pyridyl
NH	propyl	OCOOEt	2-(1-pyrrolidinyl)-3-pyridyl
NH	propyl	OCOOEt	3-(1-pyrrolidinyl)-3-pyridyl
NH	propyl	OCOOEt	5-(1-pyrrolidinyl)-3-pyridyl
NH	propyl	OCOOEt	6-(1-pyrrolidinyl)-3-pyridyl
NH	propyl	OCOOEt	2-piperidino-3-pyridyl
NH	propyl	OCOOEt	4-piperidino-3-pyridyl
NH	propyl	OCOOEt	5-piperidino-3-pyridyl
NH	propyl	OCOOEt	6-piperidino-3-pyridyl
NH	propyl	OCOOEt	2-morpholino-3-pyridyl
NH	propyl	OCOOEt	4-morpholino-3-pyridyl
NH	propyl	OCOOEt	5-morpholino-3-pyridyl
NH	propyl	OCOOEt	6-morpholino-3-pyridyl
NH	propyl	OCOOEt	2-hydroxy-3-pyridyl
NH	propyl	OCOOEt	4-hydroxy-3-pyridyl
NH	propyl	OCOOEt	5-hydroxy-3-pyridyl
NH	propyl	OCOOEt	6-hydroxy-3-pyridyl
NH	propyl	OCOOEt	2-mercapto-3-pyridyl
NH	propyl	OCOOEt	4-mercapto-3-pyridyl
NH	propyl	OCOOEt	5-mercapto-3-pyridyl
NH	propyl	OCOOEt	6-mercapto-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	propyl	OCOOEt	2-methylthio-3-pyridyl
NH	propyl	OCOOEt	4-methylthio-3-pyridyl
NH	propyl	OCOOEt	5-methylthio-3-pyridyl
NH	propyl	OCOOEt	6-methylthio-3-pyridyl
NH	propyl	OCOOEt	2,6-dimethyl-3-pyridyl
NH	propyl	OCOOEt	5,6-dimethyl-3-pyridyl
NH	propyl	OCOOEt	2,6-diethyl-3-pyridyl
NH	propyl	OCOOEt	5,6-diethyl-3-pyridyl
NH	propyl	OCOOEt	2,6-dimethoxy-3-pyridyl
NH	propyl	OCOOEt	5,6-dimethoxy-3-pyridyl
NH	propyl	OCOOEt	2,6-diethoxy-3-pyridyl
NH	propyl	OCOOEt	5,6-diethoxy-3-pyridyl
NH	propyl	OCOOEt	2,6-dichloro-3-pyridyl
NH	propyl	OCOOEt	5,6-dichloro-3-pyridyl
NH	propyl	OCOOEt	5-chloro-6-methoxy-3-pyridyl
NH	propyl	OCOOEt	5-chloro-6-ethoxy-3-pyridyl
NH	propyl	OCOOEt	2-chloro-6-methyl-3-pyridyl
NH	propyl	OCOOEt	6-chloro-2-methyl-3-pyridyl
NH	propyl	OCOOEt	2-methyl-4-pyridyl
NH	propyl	OCOOEt	2-ethyl-4-pyridyl
NH	propyl	OCOOEt	2-methoxy-4-pyridyl
NH	propyl	OCOOEt	2-ethoxy-4-pyridyl
NH	propyl	OCOOEt	2-chloro-4-pyridyl
NH	propyl	OCOOEt	2-dimethylamino-4-pyridyl
NH	propyl	OCOOEt	2-(1-pyrrolidinyl)-4-pyridyl
NH	propyl	OCOOEt	2-piperidino-4-pyridyl
NH	propyl	OCOOEt	2-morpholino-4-pyridyl
NH	propyl	OCOOEt	2-methylthio-4-pyridyl
NH	propyl	OCOOEt	2-pyrazinyl
NH	propyl	OCOOEt	5-methyl-2-pyrazinyl
NH	propyl	OCOOEt	5-ethyl-2-pyrazinyl
NH	propyl	OCOOEt	5-methoxy-2-pyrazinyl
NH	propyl	OCOOEt	5-ethoxy-2-pyrazinyl
NH	propyl	OCOOEt	5-chloro-2-pyrazinyl
NH	propyl	OCOOEt	6-methyl-2-pyrazinyl
NH	propyl	OCOOEt	6-methoxy-2-pyrazinyl
NH	propyl	OCOOEt	6-chloro-2-pyrazinyl
NH	n-butyl	OH	2-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-butyl	OH	3-pyridyl
NH	n-butyl	OH	4-pyridyl
NH	n-butyl	OH	2-methyl-3-pyridyl
NH	n-butyl	OH	4-methyl-3-pyridyl
NH	n-butyl	OH	5-methyl-3-pyridyl
NH	n-butyl	OH	6-methyl-3-pyridyl
NH	n-butyl	OH	2-ethyl-3-pyridyl
NH	n-butyl	OH	4-ethyl-3-pyridyl
NH	n-butyl	OH	5-ethyl-3-pyridyl
NH	n-butyl	OH	6-ethyl-3-pyridyl
NH	n-butyl	OH	2-methoxy-3-pyridyl
NH	n-butyl	OH	4-methoxy-3-pyridyl
NH	n-butyl	OH	6-methoxy-3-pyridyl
NH	n-butyl	OH	6-methoxy-3-pyridyl
NH	n-butyl	OH	2-ethoxy-3-pyridyl
NH	n-butyl	OH	4-ethoxy-3-pyridyl
NH	n-butyl	OH	5-ethoxy-3-pyridyl
NH	n-butyl	OH	6-ethoxy-3-pyridyl
NH	n-butyl	OH	2-chloro-3-pyridyl
NH	n-butyl	OH	4-chloro-3-pyridyl
NH	n-butyl	OH	5-chloro-3-pyridyl
NH	n-butyl	OH	6-chloro-3-pyridyl
NH	n-butyl	OH	2-fluoro-3-pyridyl
NH	n-butyl	OH	4-fluoro-3-pyridyl
NH	n-butyl	OH	5-fluoro-3-pyridyl
NH	n-butyl	OH	6-fluoro-3-pyridyl
NH	n-butyl	OH	2-dimethylamino-3-pyridyl
NH	n-butyl	OH	4-dimethylamino-3-pyridyl
NH	n-butyl	OH	5-dimethylamino-3-pyridyl
NH	n-butyl	OH	6-dimethylamino-3-pyridyl
NH	n-butyl	OH	2-(1-pyrrolidinyl)-3-pyridyl
NH	n-butyl	OH	3-(1-pyrrolidinyl)-3-pyridyl
NH	n-butyl	OH	5-(1-pyrrolidinyl)-3-pyridyl
NH	n-butyl	OH	6-(1-pyrrolidinyl)-3-pyridyl
NH	n-butyl	OH	2-piperidino-3-pyridyl
NH	n-butyl	OH	4-piperidino-3-pyridyl
NH	n-butyl	OH	5-piperidino-3-pyridyl
NH	n-butyl	OH	6-piperidino-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-butyl	OH	2-morpholino-3-pyridyl
NH	n-butyl	OH	4-morpholino-3-pyridyl
NH	n-butyl	OH	5-morpholino-3-pyridyl
NH	n-butyl	OH	6-morpholino-3-pyridyl
NH	n-butyl	OH	2-hydroxy-3-pyridyl
NH	n-butyl	OH	4-hydroxy-3-pyridyl
NH	n-butyl	OH	5-hydroxy-3-pyridyl
NH	n-butyl	OH	6-hydroxy-3-pyridyl
NH	n-butyl	OH	2-mercapto-3-pyridyl
NH	n-butyl	OH	4-mercapto-3-pyridyl
NH	n-butyl	OH	5-mercapto-3-pyridyl
NH	n-butyl	OH	6-mercapto-3-pyridyl
NH	n-butyl	OH	2-methylthio-3-pyridyl
NH	n-butyl	OH	4-methylthio-3-pyridyl
NH	n-butyl	OH	5-methylthio-3-pyridyl
NH	n-butyl	OH	6-methylthio-3-pyridyl
NH	n-butyl	OH	2,6-dimethyl-3-pyridyl
NH	n-butyl	OH	5,6-dimethyl-3-pyridyl
NH	n-butyl	OH	2,6-diethyl-3-pyridyl
NH	n-butyl	OH	5,6-diethyl-3-pyridyl
NH	n-butyl	OH	2,6-dimethoxy-3-pyridyl
NH	n-butyl	OH	5,6-dimethoxy-3-pyridyl
NH	n-butyl	OH	2,6-diethoxy-3-pyridyl
NH	n-butyl	OH	5,6-diethoxy-3-pyridyl
NH	n-butyl	OH	2,6-dichloro-3-pyridyl
NH	n-butyl	OH	5,6-dichloro-3-pyridyl
NH	n-butyl	OH	5-chloro-6-methoxy-3-pyridyl
NH	n-butyl	OH	5-chloro-6-ethoxy-3-pyridyl
NH	n-butyl	OH	2-chloro-6-methyl-3-pyridyl
NH	n-butyl	OH	6-chloro-2-methyl-3-pyridyl
NH	n-butyl	OH	2-methyl-4-pyridyl
NH	n-butyl	OH	2-ethyl-4-pyridyl
NH	n-butyl	OH	2-methoxy-4-pyridyl
NH	n-butyl	OH	2-ethoxy-4-pyridyl
NH	n-butyl	OH	2-chloro-4-pyridyl
NH	n-butyl	OH	2-dimethylamino-4-pyridyl
NH	n-butyl	OH	2-(1-pyrrolidinyl)-4-pyridyl
NH	n-butyl	OH	2-piperidino-4-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-butyl	OH	2-morpholino-4-pyridyl
NH	n-butyl	OH	2-methylthio-4-pyridyl
NH	n-butyl	OH	2-pyrazinyl
NH	n-butyl	OH	5-methyl-2-pyrazinyl
NH	n-butyl	OH	5-ethyl-2-pyrazinyl
NH	n-butyl	OH	5-methoxy-2-pyrazinyl
NH	n-butyl	OH	5-ethoxy-2-pyrazinyl
NH	n-butyl	OH	5-chloro-2-pyrazinyl
NH	n-butyl	OH	6-methyl-2-pyrazinyl
NH	n-butyl	OH	6-methoxy-2-pyrazinyl
NH	n-butyl	OH	6-chloro-2-pyrazinyl
NH	n-butyl	OCOOMe	2-pyridyl
NH	n-butyl	OCOOMe	3-pyridyl
NH	n-butyl	OCOOMe	4-pyridyl
NH	n-butyl	OCOOMe	2-methyl-3-pyridyl
NH	n-butyl	OCOOMe	4-methyl-3-pyridyl
NH	n-butyl	OCOOMe	5-methyl-3-pyridyl
NH	n-butyl	OCOOMe	6-methyl-3-pyridyl
NH	n-butyl	OCOOMe	2-ethyl-3-pyridyl
NH	n-butyl	OCOOMe	4-ethyl-3-pyridyl
NH	n-butyl	OCOOMe	5-ethyl-3-pyridyl
NH	n-butyl	OCOOMe	6-ethyl-3-pyridyl
NH	n-butyl	OCOOMe	2-methoxy-3-pyridyl
NH	n-butyl	OCOOMe	4-methoxy-3-pyridyl
NH	n-butyl	OCOOMe	5-methoxy-3-pyridyl
NH	n-butyl	OCOOMe	6-methoxy-8-pyridyl
NH	n-butyl	OCOOMe	2-ethoxy-3-pyridyl
NH	n-butyl	OCOOMe	4-ethoxy-3-pyridyl
NH	n-butyl	OCOOMe	5-ethoxy-3-pyridyl
NH	n-butyl	OCOOMe	6-ethoxy-3-pyridyl
NH	n-butyl	OCOOMe	2-chloro-3-pyridyl
NH	n-butyl	OCOOMe	4-chloro-3-pyridyl
NH	n-butyl	OCOOMe	5-chloro-3-pyridyl
NH	n-butyl	OCOOMe	6-chloro-3-pyridyl
NH	n-butyl	OCOOMe	2-fluoro-3-pyridyl
NH	n-butyl	OCOOMe	4-fluoro-3-pyridyl
NH	n-butyl	OCOOMe	5-fluoro-3-pyridyl
NH	n-butyl	OCOOMe	6-fluoro-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-butyl	OCOOMe	2-dimethylamino-3-pyridyl
NH	n-butyl	OCOOMe	4-dimethylamino-3-pyridyl
NH	n-butyl	OCOOMe	5-dimethylamino-3-pyridyl
NH	n-butyl	OCOOMe	6-dimethylamino-3-pyridyl
NH	n-butyl	OCOOMe	2-(1-pyrrolidinyl)-3-pyridyl
NH	n-butyl	OCOOMe	3-(1-pyrrolidinyl)-3-pyridyl
NH	n-butyl	OCOOMe	5-(1-pyrrolidinyl)-3-pyridyl
NH	n-butyl	OCOOMe	6-(1-pyrrolidinyl)-3-pyridyl
NH	n-butyl	OCOOMe	2-piperidino-3-pyridyl
NH	n-butyl	OCOOMe	4-piperidino-3-pyridyl
NH	n-butyl	OCOOMe	5-piperidino-3-pyridyl
NH	n-butyl	OCOOMe	6-piperidino-3-pyridyl
NH	n-butyl	OCOOMe	2-morpholino-3-pyridyl
NH	n-butyl	OCOOMe	4-morpholino-3-pyridyl
NH	n-butyl	OCOOMe	5-morpholino-3-pyridyl
NH	n-butyl	OCOOMe	6-morpholino-3-pyridyl
NH	n-butyl	OCOOMe	2-hydroxy-3-pyridyl
NH	n-butyl	OCOOMe	4-hydroxy-3-pyridyl
NH	n-butyl	OCOOMe	5-hydroxy-3-pyridyl
NH	n-butyl	OCOOMe	6-hydroxy-3-pyridyl
NH	n-butyl	OCOOMe	2-mercapto-3-pyridyl
NH	n-butyl	OCOOMe	4-mercapto-3-pyridyl
NH	n-butyl	OCOOMe	5-mercapto-3-pyridyl
NH	n-butyl	OCOOMe	6-mercapto-3-pyridyl
NH	n-butyl	OCOOMe	2-methylthio-3-pyridyl
NH	n-butyl	OCOOMe	4-methylthio-3-pyridyl
NH	n-butyl	OCOOMe	5-methylthio-3-pyridyl
NH	n-butyl	OCOOMe	6-methylthio-3-pyridyl
NH	n-butyl	OCOOMe	2,6-dimethyl-3-pyridyl
NH	n-butyl	OCOOMe	5,6-dimethyl-3-pyridyl
NH	n-butyl	OCOOMe	2,6-diethyl-3-pyridyl
NH	n-butyl	OCOOMe	5,6-diethyl-3-pyridyl
NH	n-butyl	OCOOMe	2,6-dimethoxy-3-pyridyl
NH	n-butyl	OCOOMe	5,6-dimethoxy-3-pyridyl
NH	n-butyl	OCOOMe	2,6-diethoxy-3-pyridyl
NH	n-butyl	OCOOMe	5,6-diethoxy-3-pyridyl
NH	n-butyl	OCOOMe	2,6-dichloro-3-pyridyl
NH	n-butyl	OCOOMe	5,6-dichloro-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-butyl	OCOOMe	5-chloro-6-methoxy-3-pyridyl
NH	n-butyl	OCOOMe	5-chloro-6-ethoxy-3-pyridyl
NH	n-butyl	OCOOMe	2-chloro-6-methyl-3-pyridyl
NH	n-butyl	OCOOMe	6-chloro-2-methyl-3-pyridyl
NH	n-butyl	OCOOMe	2-methyl-4-pyridyl
NH	n-butyl	OCOOMe	2-ethyl-4-pyridyl
NH	n-butyl	OCOOMe	2-methoxy-4-pyridyl
NH	n-butyl	OCOOMe	2-ethoxy-4-pyridyl
NH	n-butyl	OCOOMe	2-chloro-4-pyridyl
NH	n-butyl	OCOOMe	2-dimethylamino-4-pyridyl
NH	n-butyl	OCOOMe	2-(1-pyrrolidinyl)-4-pyridyl
NH	n-butyl	OCOOMe	2-piperidino-4-pyridyl
NH	n-butyl	OCOOMe	2-morpholino-4-pyridyl
NH	n-butyl	OCOOMe	2-methylthio-4-pyridyl
NH	n-butyl	OCOOMe	2-pyrazinyl
NH	n-butyl	OCOOMe	5-methyl-2-pyrazinyl
NH	n-butyl	OCOOMe	5-ethyl-2-pyrazinyl
NH	n-butyl	OCOOMe	5-methoxy-2-pyrazinyl
NH	n-butyl	OCOOMe	5-ethoxy-2-pyrazinyl
NH	n-butyl	OCOOMe	5-chloro-2-pyrazinyl
NH	n-butyl	OCOOMe	6-methyl-2-pyrazinyl
NH	n-butyl	OCOOMe	6-methoxy-2-pyrazinyl
NH	n-butyl	OCOOMe	6-chloro-2-pyrazinyl
NH	n-butyl	OCOOEt	2-pyridyl
NH	n-butyl	OCOOEt	3-pyridyl
NH	n-butyl	OCOOEt	4-pyridyl
NH	n-butyl	OCOOEt	2-methyl-3-pyridyl
NH	n-butyl	OCOOEt	4-methyl-3-pyridyl
NH	n-butyl	OCOOEt	5-methyl-3-pyridyl
NH	n-butyl	OCOOEt	6-methyl-3-pyridyl
NH	n-butyl	OCOOEt	2-ethyl-3-pyridyl
NH	n-butyl	OCOOEt	4-ethyl-3-pyridyl
NH	n-butyl	OCOOEt	5-ethyl-3-pyridyl
NH	n-butyl	OCOOEt	6-ethyl-3-pyridyl
NH	n-butyl	OCOOEt	2-methoxy-3-pyridyl
NH	n-butyl	OCOOEt	4-methoxy-3-pyridyl
NH	n-butyl	OCOOEt	5-methoxy-3-pyridyl
NH	n-butyl	OCOOEt	6-methoxy-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-butyl	OCOOEt	2-ethoxy-3-pyridyl
NH	n-butyl	OCOOEt	4-ethoxy-3-pyridyl
NH	n-butyl	OCOOEt	5-ethosy-3-pyridyl
NH	n-butyl	OCOOEt	6-ethoxy-3-pyridyl
NH	n-butyl	OCOOEt	2-chloro-3-pyridyl
NH	n-butyl	OCOOEt	4-chloro-3-pyridyl
NH	n-butyl	OCOOEt	5-chloro-3-pyridyl
NH	n-butyl	OCOOEt	6-chloro-3-pyridyl
NH	n-butyl	OCOOEt	2-fluoro-3-pyridyl
NH	n-butyl	OCOOEt	4-fluoro-3-pyridyl
NH	n-butyl	OCOOEt	5-fluoro-3-pyridyl
NH	n-butyl	OCOOEt	6-fluoro-3-pyridyl
NH	n-butyl	OCOOEt	2-dimethylamino-3-pyridyl
NH	n-butyl	OCOOEt	4-dimethylamino-3-pyridyl
NH	n-butyl	OCOOEt	5-dimethylamino-3-pyridyl
NH	n-butyl	OCOOEt	6-dimethylamino-3-pyridyl
NH	n-butyl	OCOOEt	2-(1-pyrrolidinyl)-3-pyridyl
NH	n-butyl	OCOOEt	3-(1-pyrrolidinyl)-3-pyridyl
NH	n-butyl	OCOOEt	5-(1-pyrrolidinyl)-3-pyridyl
NH	n-butyl	OCOOEt	6-(1-pyrrolidinyl)-3-pyridyl
NH	n-butyl	OCOOEt	2-piperidino-3-pyridyl
NH	n-butyl	OCOOEt	4-piperidino-3-pyridyl
NH	n-butyl	OCOOEt	5-piperidino-3-pyridyl
NH	n-butyl	OCOOEt	6-piperidino-3-pyridyl
NH	n-butyl	OCOOEt	2-morpholino-3-pyridyl
NH	n-butyl	OCOOEt	4-morpholino-3-pyridyl
NH	n-butyl	OCOOEt	5-morpholino-3-pyridyl
NH	n-butyl	OCOOEt	6-morpholino-3-pyridyl
NH	n-butyl	OCOOEt	2-hydroxy-3-pyridyl
NH	n-butyl	OCOOEt	4-hydroxy-3-pyridyl
NH	n-butyl	OCOOEt	5-hydroxy-3-pyridyl
NH	n-butyl	OCOOEt	6-hydroxy-3-pyridyl
NH	n-butyl	OCOOEt	2-mercapto-3-pyridyl
NH	n-butyl	OCOOEt	4-mercapto-3-pyridyl
NH	n-butyl	OCOOEt	5-mercapto-3-pyridyl
NH	n-butyl	OCOOEt	6-mercapto-3-pyridyl
NH	n-butyl	OCOOEt	2-methylthio-3-pyridyl
NH	n-butyl	OCOOEt	4-methylthio-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-butyl	OCOOEt	5-methylthio-3-pyridyl
NH	n-butyl	OCOOEt	6-methylthio-3-pyridyl
NH	n-butyl	OCOOEt	2,6-dimethyl-3-pyridyl
NH	n-butyl	OCOOEt	5,6-dimethyl-3-pyridyl
NH	n-butyl	OCOOEt	2,6-diethyl-3-pyridyl
NH	n-butyl	OCOOEt	5,6-diethyl-3-pyridyl
NH	n-butyl	OCOOEt	2,6-dimethoxy-3-pyridyl
NH	n-butyl	OCOOEt	5,6-dimethoxy-3-pyridyl
NH	n-butyl	OCOOEt	2,6-diethoxy-3-pyridyl
NH	n-butyl	OCOOEt	5,6-diethoxy-3-pyridyl
NH	n-butyl	OCOOEt	2,6-dichloro-3-pyridyl
NH	n-butyl	OCOOEt	5,6-dichloro-3-pyridyl
NH	n-butyl	OCOOEt	5-chloro-6-methoxy-3-pyridyl
NH	n-butyl	OCOOEt	5-chloro-6-ethoxy-3-pyridyl
NH	n-butyl	OCOOEt	2-chloro-6-methyl-3-pyridyl
NH	n-butyl	OCOOEt	6-chloro-2-methyl-3-pyridyl
NH	n-butyl	OCOOEt	2-methyl-4-pyridyl
NH	n-butyl	OCOOEt	2-ethyl-4-pyridyl
NH	n-butyl	OCOOEt	2-methoxy-4-pyridyl
NH	n-butyl	OCOOEt	2-ethoxy-4-pyridyl
NH	n-butyl	OCOOEt	2-chloro-4-pyridyl
NH	n-butyl	OCOOEt	2-dimethylamino-4-pyridyl
NH	n-butyl	OCOOEt	2-(1-pyrrolidinyl)-4-pyridyl
NH	n-butyl	OCOOEt	2-piperidino-4-pyridyl
NH	n-butyl	OCOOEt	2-morpholino-4-pyridyl
NH	n-butyl	OCOOEt	2-methylthio-4-pyridyl
NH	n-butyl	OCOOEt	2-pyrazinyl
NH	n-butyl	OCOOEt	5-methyl-2-pyrazinyl
NH	n-butyl	OCOOEt	5-ethyl-2-pyrazinyl
NH	n-butyl	OCOOEt	5-methoxy-2-pyrazinyl
NH	n-butyl	OCOOEt	5-ethoxy-2-pyrazinyl
NH	n-butyl	OCOOEt	5-chloro-2-pyrazinyl
NH	n-butyl	OCOOEt	6-methyl-2-pyrazinyl
NH	n-butyl	OCOOEt	6-methoxy-2-pyrazinyl
NH	n-butyl	OCOOEt	6-chloro-2-pyrazinyl
NH	n-pentyl	OH	2-pyridyl
NH	n-pentyl	OH	3-pyridyl
NH	n-pentyl	OH	4-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-pentyl	OH	2-methyl-3-pyridyl
NH	n-pentyl	OH	4-methyl-3-pyridyl
NH	n-pentyl	OH	5-methyl-3-pyridyl
NH	n-pentyl	OH	6-methyl-3-pyridyl
NH	n-pentyl	OH	2-ethyl-3-pyridyl
NH	n-pentyl	OH	4-ethyl-3-pyridyl
NH	n-pentyl	OH	5-ethyl-3-pyridyl
NH	n-pentyl	OH	6-ethyl-3-pyridyl
NH	n-pentyl	OH	2-methoxy-3-pyridyl
NH	n-pentyl	OH	4-methoxy-3-pyridyl
NH	n-pentyl	OH	5-methoxy-3-pyridyl
NH	n-pentyl	OH	6-methoxy-3-pyridyl
NH	n-pentyl	OH	2-ethoxy-3-pyridyl
NH	n-pentyl	OH	4-ethoxy-3-pyridyl
NH	n-pentyl	OH	5-ethoxy-3-pyridyl
NH	n-pentyl	OH	6-ethoxy-3-pyridyl
NH	n-pentyl	OH	2-chloro-3-pyridyl
NH	n-pentyl	OH	4-chloro-3-pyridyl
NH	n-pentyl	OH	5-chloro-3-pyridyl
NH	n-pentyl	OH	6-chloro-3-pyridyl
NH	n-pentyl	OH	2-fluoro-3-pyridyl
NH	n-pentyl	OH	4-fluoro-3-pyridyl
NH	n-pentyl	OH	5-fluoro-3-pyridyl
NH	n-pentyl	OH	6-fluoro-3-pyridyl
NH	n-pentyl	OH	2-dimethylamino-3-pyridyl
NH	n-pentyl	OH	4-dimethylamino-3-pyridyl
NH	n-pentyl	OH	5-dimethylamino-3-pyridyl
NH	n-pentyl	OH	6-dimethylamino-3-pyridyl
NH	n-pentyl	OH	2-(1-pyrrolidinyl)-3-pyridyl
NH	n-pentyl	OH	3-(1-pyrrolidinyl)-3-pyridyl
NH	n-pentyl	OH	5-(1-pyrrolidinyl)-3-pyridyl
NH	n-pentyl	OH	6-(1-pyrrolidinyl)-3-pyridyl
NH	n-pentyl	OH	2-piperidino-3-pyridyl
NH	n-pentyl	OH	4-piperidino-3-pyridyl
NH	n-pentyl	OH	5-piperidino-3-pyridyl
NH	n-pentyl	OH	6-piperidino-3-pyridyl
NH	n-pentyl	OH	2-morpholino-3-pyridyl
NH	n-pentyl	OH	4-morpholino-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-pentyl	OH	5-morpholino-3-pyridyl
NH	n-pentyl	OH	6-morpholino-3-pyridyl
NH	n-pentyl	OH	2-hydroxy-3-pyridyl
NH	n-pentyl	OH	4-hydroxy-3-pyridyl
NH	n-pentyl	OH	5-hydroxy-3-pyridyl
NH	n-pentyl	OH	6-hydroxy-3-pyridyl
NH	n-pentyl	OH	2-mercapto-3-pyridyl
NH	n-pentyl	OH	4-mercapto-3-pyridyl
NH	n-pentyl	OH	5-mercapto-3-pyridyl
NH	n-pentyl	OH	6-mercapto-3-pyridyl
NH	n-pentyl	OH	2-methylthio-3-pyridyl
NH	n-pentyl	OH	4-methylthio-3-pyridyl
NH	n-pentyl	OH	5-methylthio-3-pyridyl
NH	n-pentyl	OH	6-methylthio-3-pyridyl
NH	n-pentyl	OH	2,6-dimethyl-3-pyridyl
NH	n-pentyl	OH	5,6-dimethyl-3-pyridyl
NH	n-pentyl	OH	2,6-diethyl-3-pyridyl
NH	n-pentyl	OH	5,6-diethyl-3-pyridyl
NH	n-pentyl	OH	2,6-dimethoxy-3-pyridyl
NH	n-pentyl	OH	5,6-dimethoxy-3-pyridyl
NH	n-pentyl	OH	2,6-diethoxy-3-pyridyl
NH	n-pentyl	OH	5,6-diethoxy-3-pyridyl
NH	n-pentyl	OH	2,6-dichloro-3-pyridyl
NH	n-pentyl	OH	5,6-dichloro-3-pyridyl
NH	n-pentyl	OH	5-chloro-6-methoxy-3-pyridyl
NH	n-pentyl	OH	5-chloro-6-ethoxy-3-pyridyl
NH	n-pentyl	OH	2-chloro-6-methyl-3-pyridyl
NH	n-pentyl	OH	6-chloro-2-methyl-3-pyridyl
NH	n-pentyl	OH	2-methyl-4-pyridyl
NH	n-pentyl	OH	2-ethyl-4-pyridyl
NH	n-pentyl	OH	2-methoxy-4-pyridyl
NH	n-pentyl	OH	2-ethoxy-4-pyridyl
NH	n-pentyl	OH	2-chloro-4-pyridyl
NH	n-pentyl	OH	2-dimethylamino-4-pyridyl
NH	n-pentyl	OH	2-(1-pyrrolidinyl)-4-pyridyl
NH	n-pentyl	OH	2-piperidino-4-pyridyl
NH	n-pentyl	OH	2-morpholino-4-pyridyl
NH	n-pentyl	OH	2-methylthio-4-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-pentyl	OH	2-pyrazinyl
NH	n-pentyl	OH	5-methyl-2-pyrazinyl
NH	n-pentyl	OH	5-ethyl-2-pyrazinyl
NH	n-pentyl	OH	5-methoxy-2-pyrazinyl
NH	n-pentyl	OH	5-ethoxy-2-pyrazinyl
NH	n-pentyl	OH	5-chloro-2-pyrazinyl
NH	n-pentyl	OH	6-methyl-2-pyrazinyl
NH	n-pentyl	OH	6-methoxy-2-pyrazinyl
NH	n-pentyl	OH	6-chloro-2-pyrazinyl
NH	n-pentyl	OCOOMe	2-pyridyl
NH	n-pentyl	OCOOMe	3-pyridyl
NH	n-pentyl	OCOOMe	4-pyridyl
NH	n-pentyl	OCOOMe	2-methyl-3-pyridyl
NH	n-pentyl	OCOOMe	4-methyl-3-pyridyl
NH	n-pentyl	OCOOMe	5-methyl-3-pyridyl
NH	n-pentyl	OCOOMe	6-methyl-3-pyridyl
NH	n-pentyl	OCOOMe	2-ethyl-3-pyridyl
NH	n-pentyl	OCOOMe	4-ethyl-3-pyridyl
NH	n-pentyl	OCOOMe	5-ethyl-3-pyridyl
NH	n-pentyl	OCOOMe	6-ethyl-3-pyridyl
NH	n-pentyl	OCOOMe	2-methoxy-3-pyridyl
NH	n-pentyl	OCOOMe	4-methoxy-3-pyridyl
NH	n-pentyl	OCOOMe	5-methoxy-3-pyridyl
NH	n-pentyl	OCOOMe	6-methoxy-3-pyridyl
NH	n-pentyl	OCOOMe	2-ethoxy-3-pyridyl
NH	n-pentyl	OCOOMe	4-ethoxy-3-pyridyl
NH	n-pentyl	OCOOMe	5-ethoxy-3-pyridyl
NH	n-pentyl	OCOOMe	6-ethoxy-3-pyridyl
NH	n-pentyl	OCOOMe	2-chloro-3-pyridyl
NH	n-pentyl	OCOOMe	4-chloro-3-pyridyl
NH	n-pentyl	OCOOMe	5-chloro-3-pyridyl
NH	n-pentyl	OCOOMe	6-chloro-3-pyridyl
NH	n-pentyl	OCOOMe	2-fluoro-3-pyridyl
NH	n-pentyl	OCOOMe	4-fluoro-3-pyridyl
NH	n-pentyl	OCOOMe	6-fluoro-3-pyridyl
NH	n-pentyl	OCOOMe	6-fluoro-3-pyridyl
NH	n-pentyl	OCOOMe	2-dimethylamino-3-pyridyl
NH	n-pentyl	OCOOMe	4-dimethylamino-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-pentyl	OCOOMe	5-dimethylamino-3-pyridyl
NH	n-pentyl	OCOOMe	6-dimethylamino-3-pyridyl
NH	n-pentyl	OCOOMe	2-(1-pyrrolidinyl)-3-pyridyl
NH	n-pentyl	OCOOMe	3-(1-pyrrolidinyl)-3-pyridyl
NH	n-pentyl	OCOOMe	5-(1-pyrrolidinyl)-3-pyridyl
NH	n-pentyl	OCOOMe	6-(1-pyrrolidinyl)-3-pyridyl
NH	n-pentyl	OCOOMe	2-piperidino-3-pyridyl
NH	n-pentyl	OCOOMe	4-piperidino-3-pyridyl
NH	n-pentyl	OCOOMe	5-piperidino-3-pyridyl
NH	n-pentyl	OCOOMe	6-piperidino-3-pyridyl
NH	n-pentyl	OCOOMe	2-morpholino-3-pyridyl
NH	n-pentyl	OCOOMe	4-morpholino-3-pyridyl
NH	n-pentyl	OCOOMe	5-morpholino-3-pyridyl
NH	n-pentyl	OCOOMe	6-morpholino-3-pyridyl
NH	n-pentyl	OCOOMe	2-hydroxy-3-pyridyl
NH	n-pentyl	OCOOMe	4-hydroxy-3-pyridyl
NH	n-pentyl	OCOOMe	5-hydroxy-3-pyridyl
NH	n-pentyl	OCOOMe	6-hydroxy-3-pyridyl
NH	n-pentyl	OCOOMe	2-mercapto-3-pyridyl
NH	n-pentyl	OCOOMe	4-mercapto-3-pyridyl
NH	n-pentyl	OCOOMe	5-mercapto-3-pyridyl
NH	n-pentyl	OCOOMe	6-mercapto-3-pyridyl
NH	n-pentyl	OCOOMe	2-methylthio-3-pyridyl
NH	n-pentyl	OCOOMe	4-methylthio-3-pyridyl
NH	n-pentyl	OCOOMe	5-methylthio-3-pyridyl
NH	n-pentyl	OCOOMe	6-methylthio-3-pyridyl
NH	n-pentyl	OCOOMe	2,6-dimethyl-3-pyridyl
NH	n-pentyl	OCOOMe	5,6-dimethyl-3-pyridyl
NH	n-pentyl	OCOOMe	2,6-diethyl-3-pyridyl
NH	n-pentyl	OCOOMe	5,6-diethyl-3-pyridyl
NH	n-pentyl	OCOOMe	2,6-dimethoxy-3-pyridyl
NH	n-pentyl	OCOOMe	5,6-dimethoxy-3-pyridyl
NH	n-pentyl	OCOOMe	2,6-diethoxy-3-pyridyl
NH	n-pentyl	OCOOMe	5,6-diethoxy-3-pyridyl
NH	n-pentyl	OCOOMe	2,6-dichloro-3-pyridyl
NH	n-pentyl	OCOOMe	5,6-dichloro-3-pyridyl
NH	n-pentyl	OCOOMe	5-chloro-6-methoxy-3-pyridyl
NH	n-pentyl	OCOOMe	5-chloro-6-ethoxy-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-pentyl	OCOOMe	2-chloro-6-methyl-3-pyridyl
NH	n-pentyl	OCOOMe	6-chloro-2-methyl-3-pyridyl
NH	n-pentyl	OCOOMe	2-methyl-4-pyridyl
NH	n-pentyl	OCOOMe	2-ethyl-4-pyridyl
NH	n-pentyl	OCOOMe	2-methoxy-4-pyridyl
NH	n-pentyl	OCOOMe	2-ethoxy-4-pyridyl
NH	n-pentyl	OCOOMe	2-chloro-4-pyridyl
NH	n-pentyl	OCOOMe	2-dimethylamino-4-pyridyl
NH	n-pentyl	OCOOMe	2-(1-pyrrolidinyl)-4-pyridyl
NH	n-pentyl	OCOOMe	2-piperidino-4-pyridyl
NH	n-pentyl	OCOOMe	2-morpholino-4-pyridyl
NH	n-pentyl	OCOOMe	2-methylthio-4-pyridyl
NH	n-pentyl	OCOOMe	2-pyrazinyl
NH	n-pentyl	OCOOMe	5-methyl-2-pyrazinyl
NH	n-pentyl	OCOOMe	5-ethyl-2-pyrazinyl
NH	n-pentyl	OCOOMe	5-methoxy-2-pyrazinyl
NH	n-pentyl	OCOOMe	5-ethoxy-2-pyrazinyl
NH	n-pentyl	OCOOMe	5-chloro-2-pyrazinyl
NH	n-pentyl	OCOOMe	6-methyl-2-pyrazinyl
NH	n-pentyl	OCOOMe	6-methoxy-2-pyrazinyl
NH	n-pentyl	OCOOMe	6-chloro-2-pyrazinyl
NH	n-pentyl	OCOOEt	2-pyridyl
NH	n-pentyl	OCOOEt	3-pyridyl
NH	n-pentyl	OCOOEt	4-pyridyl
NH	n-pentyl	OCOOEt	2-methyl-3-pyridyl
NH	n-pentyl	OCOOEt	4-methyl-3-pyridyl
NH	n-pentyl	OCOOEt	5-methyl-3-pyridyl
NH	n-pentyl	OCOOEt	6-methyl-3-pyridyl
NH	n-pentyl	OCOOEt	2-ethyl-3-pyridyl
NH	n-pentyl	OCOOEt	4-ethyl-3-pyridyl
NH	n-pentyl	OCOOEt	5-ethyl-3-pyridyl
NH	n-pentyl	OCOOEt	6-ethyl-3-pyridyl
NH	n-pentyl	OCOOEt	2-methoxy-3-pyridyl
NH	n-pentyl	OCOOEt	4-methoxy-3-pyridyl
NH	n-pentyl	OCOOEt	5-methoxy-3-pyridyl
NH	n-pentyl	OCOOEt	6-methoxy-3-pyridyl
NH	n-pentyl	OCOOEt	2-ethoxy-3-pyridyl
NH	n-pentyl	OCOOEt	4-ethoxy-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-pentyl	OCOOEt	5-ethoxy-3-pyridyl
NH	n-pentyl	OCOOEt	6-ethoxy-3-pyridyl
NH	n-pentyl	OCOOEt	2-chloro-3-pyridyl
NH	n-pentyl	OCOOEt	4-chloro-3-pyridyl
NH	n-pentyl	OCOOEt	5-chloro-3-pyridyl
NH	n-pentyl	OCOOEt	6-chloro-3-pyridyl
NH	n-pentyl	OCOOEt	2-fluoro-3-pyridyl
NH	n-pentyl	OCOOEt	4-fluoro-3-pyridyl
NH	n-pentyl	OCOOEt	5-fluoro-3-pyridyl
NH	n-pentyl	OCOOEt	6-fluoro-3-pyridyl
NH	n-pentyl	OCOOEt	2-dimethylamino-3-pyridyl
NH	n-pentyl	OCOOEt	4-dimethylamino-3-pyridyl
NH	n-pentyl	OCOOEt	5-dimethylamino-3-pyridyl
NH	n-pentyl	OCOOEt	6-dimethylamino-3-pyridyl
NH	n-pentyl	OCOOEt	2-(1-pyrrolidinyl)-3-pyridyl
NH	n-pentyl	OCOOEt	3-(1-pyrrolidinyl)-3-pyridyl
NH	n-pentyl	OCOOEt	5-(1-pyrrolidinyl)-3-pyridyl
NH	n-pentyl	OCOOEt	6-(1-pyrrolidinyl)-3-pyridyl
NH	n-pentyl	OCOOEt	2-piperidino-3-pyridyl
NH	n-pentyl	OCOOEt	4-piperidino-3-pyridyl
NH	n-pentyl	OCOOEt	5-piperidino-3-pyridyl
NH	n-pentyl	OCOOEt	6-piperidino-3-pyridyl
NH	n-pentyl	OCOOEt	2-morpholino-3-pyridyl
NH	n-pentyl	OCOOEt	4-morpholino-3-pyridyl
NH	n-pentyl	OCOOEt	5-morpholino-3-pyridyl
NH	n-pentyl	OCOOEt	6-morpholino-3-pyridyl
NH	n-pentyl	OCOOEt	2-hydroxy-3-pyridyl
NH	n-pentyl	OCOOEt	4-hydroxy-3-pyridyl
NH	n-pentyl	OCOOEt	5-hydroxy-3-pyridyl
NH	n-pentyl	OCOOEt	6-hydroxy-3-pyridyl
NH	n-pentyl	OCOOEt	2-mercapto-3-pyridyl
NH	n-pentyl	OCOOEt	4-mercapto-3-pyridyl
NH	n-pentyl	OCOOEt	5-mercapto-3-pyridyl
NH	n-pentyl	OCOOEt	6-mercapto-3-pyridyl
NH	n-pentyl	OCOOEt	2-methylthio-3-pyridyl
NH	n-pentyl	OCOOEt	4-methylthio-3-pyridyl
NH	n-pentyl	OCOOEt	5-methylthio-3-pyridyl
NH	n-pentyl	OCOOEt	6-methylthio-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-pentyl	OCOOEt	2,6-dimethyl-3-pyridyl
NH	n-pentyl	OCOOEt	5,6-dimethyl-3-pyridyl
NH	n-pentyl	OCOOEt	2,6-diethyl-3-pyridyl
NH	n-pentyl	OCOOEt	5,6-diethyl-3-pyridyl
NH	n-pentyl	OCOOEt	2,6-dimethoxy-3-pyridyl
NH	n-pentyl	OCOOEt	5,6-dimethoxy-3-pyridyl
NH	n-pentyl	OCOOEt	2,6-diethoxy-3-pyridyl
NH	n-pentyl	OCOOEt	5,6-diethoxy-3-pyridyl
NH	n-pentyl	OCOOEt	2,6-dichloro-3-pyridyl
NH	n-pentyl	OCOOEt	5,6-dichloro-3-pyridyl
NH	n-pentyl	OCOOEt	5-chloro-6-methoxy-3-pyridyl
NH	n-pentyl	OCOOEt	5-chloro-6-ethoxy-3-pyridyl
NH	n-pentyl	OCOOEt	2-chloro-6-methyl-3-pyridyl
NH	n-pentyl	OCOOEt	6-chloro-2-methyl-3-pyridyl
NH	n-pentyl	OCOOEt	2-methyl-4-pyridyl
NH	n-pentyl	OCOOEt	2-ethyl-4-pyridyl
NH	n-pentyl	OCOOEt	2-methoxy-4-pyridyl
NH	n-pentyl	OCOOEt	2-ethoxy-4-pyridyl
NH	n-pentyl	OCOOEt	2-chloro-4-pyridyl
NH	n-pentyl	OCOOEt	2-dimethylamino-4-pyridyl
NH	n-pentyl	OCOOEt	2-(1-pyrrolidinyl)-4-pyridyl
NH	n-pentyl	OCOOEt	2-piperidino-4-pyridyl
NH	n-pentyl	OCOOEt	2-morpholino-4-pyridyl
NH	n-pentyl	OCOOEt	2-methylthio-4-pyridyl
NH	n-pentyl	OCOOEt	2-pyrazinyl
NH	n-pentyl	OCOOEt	5-methyl-2-pyrazinyl
NH	n-pentyl	OCOOEt	5-ethyl-2-pyrazinyl
NH	n-pentyl	OCOOEt	5-methoxy-2-pyrazinyl
NH	n-pentyl	OCOOEt	5-ethoxy-2-pyrazinyl
NH	n-pentyl	OCOOEt	5-chloro-2-pyrazinyl
NH	n-pentyl	OCOOEt	6-methyl-2-pyrazinyl
NH	n-pentyl	OCOOEt	6-methoxy-2-pyrazinyl
NH	n-pentyl	OCOOEt	6-chloro-2-pyrazinyl
O	propyl	OH	2-pyridyl
O	propyl	OH	3-pyridyl
O	propyl	OH	4-pyridyl
O	propyl	OH	2-methyl-3-pyridyl
O	propyl	OH	4-methyl-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	propyl	OH	5-methyl-3-pyridyl
O	propyl	OH	6-methyl-3-pyridyl
O	propyl	OH	2-ethyl-3-pyridyl
O	propyl	OH	4-ethyl-3-pyridyl
O	propyl	OH	5-ethyl-3-pyridyl
O	propyl	OH	6-ethyl-3-pyridyl
O	propyl	OH	2-methoxy-3-pyridyl
O	propyl	OH	4-methoxy-3-pyridyl
O	propyl	OH	5-methoxy-3-pyridyl
O	propyl	OH	6-methoxy-3-pyridyl
O	propyl	OH	2-ethoxy-3-pyridyl
O	propyl	OH	4-ethoxy-3-pyridyl
O	propyl	OH	5-ethoxy-3-pyridyl
O	propyl	OH	6-ethoxy-3-pyridyl
O	propyl	OH	2-chloro-3-pyridyl
O	propyl	OH	4-chloro-3-pyridyl
O	propyl	OH	5-chloro-3-pyridyl
O	propyl	OH	6-chloro-3-pyridyl
O	propyl	OH	2-fluoro-3-pyridyl
O	propyl	OH	4-fluoro-3-pyridyl
O	propyl	OH	5-fluoro-3-pyridyl
O	propyl	OH	6-fluoro-3-pyridyl
O	propyl	OH	2-dimethylamino-3-pyridyl
O	propyl	OH	4-dimethylamino-3-pyridyl
O	propyl	OH	5-dimethylamino-3-pyridyl
O	propyl	OH	6-dimethylamino-3-pyridyl
O	propyl	OH	2-(1-pyrrolidinyl)-3-pyridyl
O	propyl	OH	3-(1-pyrrolidinyl)-3-pyridyl
O	propyl	OH	5-(1-pyrrolidinyl)-3-pyridyl
O	propyl	OH	6-(1-pyrrolidinyl)-3-pyridyl
O	propyl	OH	2-piperidino-3-pyridyl
O	propyl	OH	4-piperidino-3-pyridyl
O	propyl	OH	5-piperidino-3-pyridyl
O	propyl	OH	6-piperidino-3-pyridyl
O	propyl	OH	2-morpholino-3-pyridyl
O	propyl	OH	4-morpholino-3-pyridyl
O	propyl	OH	5-morpholino-3-pyridyl
O	propyl	OH	6-morpholino-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	propyl	OH	2-hydroxy-3-pyridyl
O	propyl	OH	4-hydroxy-3-pyridyl
O	propyl	OH	5-hydioxy-3-pyridyl
O	propyl	OH	6-hydroxy-3-pyridyl
O	propyl	OH	2-mercapto-3-pyridyl
O	propyl	OH	4-mercapto-3-pyridyl
O	propyl	OH	5-mercapto-3-pyridyl
O	propyl	OH	6-mercapto-3-pyridyl
O	propyl	OH	2-methylthio-3-pyridyl
O	propyl	OH	4-methylthio-3-pyridyl
O	propyl	OH	5-methylthio-3-pyridyl
O	propyl	OH	6-methylthio-3-pyridyl
O	propyl	OH	2,6-dimethyl-3-pyridyl
O	propyl	OH	5,6-dimethyl-3-pyridyl
O	propyl	OH	2,6-diethyl-3-pyridyl
O	propyl	OH	5,6-diethyl-3-pyridyl
O	propyl	OH	2,6-dimethoxy-3-pyridyl
O	propyl	OH	5,6-dimethoxy-3-pyridyl
O	propyl	OH	2,6-diethoxy-3-pyridyl
O	propyl	OH	5,6-diethoxy-3-pyridyl
O	propyl	OH	2,6-dichloro-3-pyridyl
O	propyl	OH	5,6-dichloro-3-pyridyl
O	propyl	OH	5-chloro-6-methoxy-3-pyridyl
O	propyl	OH	5-chloro-6-ethoxy-3-pyridyl
O	propyl	OH	2-chloro-6-methyl-3-pyridyl
O	propyl	OH	6-chloro-2-methyl-3-pyridyl
O	propyl	OH	2-methyl-4-pyridyl
O	propyl	OH	2-ethyl-4-pyridyl
O	propyl	OH	2-methoxy-4-pyridyl
O	propyl	OH	2-ethoxy-4-pyridyl
O	propyl	OH	2-chloro-4-pyridyl
O	propyl	OH	2-dimethylamino-4-pyridyl
O	propyl	OH	2-(1-pyrrolidinyl)-4-pyridyl
O	propyl	OH	2-piperidino-4-pyridyl
O	propyl	OH	2-morpholino-4-pyridyl
O	propyl	OH	2-methylthio-4-pyridyl
O	propyl	OH	2-pyrazinyl
O	propyl	OH	5-methyl-2-pyrazinyl

Table 1 (continued)

X	R^1	R^2	Y
O	propyl	OH	5-ethyl-2-pyrazinyl
O	propyl	OH	5-methoxy-2-pyrazinyl
O	propyl	OH	5-ethoxy-2-pyrazinyl
O	propyl	OH	5-chloro-2-pyrazinyl
O	propyl	OH	6-methyl-2-pyrazinyl
O	propyl	OH	6-methoxy-2-pyrazinyl
O	propyl	OH	6-chloro-2-pyrazinyl
O	propyl	OCOOMe	2-pyridyl
O	propyl	OCOOMe	3-pyridyl
O	propyl	OCOOMe	4-pyridyl
O	propyl	OCOOMe	2-methyl-3-pyridyl
O	propyl	OCOOMe	4-methyl-3-pyridyl
O	propyl	OCOOMe	5-methyl-3-pyridyl
O	propyl	OCOOMe	6-methyl-3-pyridyl
O	propyl	OCOOMe	2-ethyl-3-pyridyl
O	propyl	OCOOMe	4-ethyl-3-pyridyl
O	propyl	OCOOMe	5-ethyl-3-pyridyl
O	propyl	OCOOMe	6-ethyl-3-pyridyl
O	propyl	OCOOMe	2-methoxy-3-pyridyl
O	propyl	OCOOMe	4-methoxy-3-pyridyl
O	propyl	OCOOMe	5-methoxy-3-pyridyl
O	propyl	OCOOMe	6-methoxy-3-pyridyl
O	propyl	OCOOMe	2-ethoxy-3-pyridyl
O	propyl	OCOOMe	4-ethoxy-3-pyridyl
O	propyl	OCOOMe	5-ethoxy-3-pyridyl
O	propyl	OCOOMe	6-ethoxy-3-pyridyl
O	propyl	OCOOMe	2-chloro-3-pyridyl
O	propyl	OCOOMe	4-chloro-3-pyridyl
O	propyl	OCOOMe	5-chloro-3-pyridyl
O	propyl	OCOOMe	6-chloro-3-pyridyl
O	propyl	OCOOMe	2-fluoro-3-pyridyl
O	propyl	OCOOMe	4-fluoro-3-pyridyl
O	propyl	OCOOMe	5-fluoro-3-pyridyl
O	propyl	OCOOMe	6-fluoro-3-pyridyl
O	propyl	OCOOMe	2-dimethylamino-3-pyridyl
O	propyl	OCOOMe	4-dimethylamino-3-pyridyl
O	propyl	OCOOMe	5-dimethylamino-3-pyridyl
O	propyl	OCOOMe	6-dimethylamino-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	propyl	OCOOMe	2-(1-pyrrolidinyl)-3-pyridyl
O	propyl	OCOOMe	3-(1-pyrrolidinyl)-3-pyridyl
O	propyl	OCOOMe	5-(1-pyrrolidinyl)-3-pyridyl
O	propyl	OCOOMe	6-(1-pyrrolidinyl)-3-pyridyl
O	propyl	OCOOMe	2-piperidino-3-pyridyl
O	propyl	OCOOMe	4-piperidino-3-pyridyl
O	propyl	OCOOMe	5-piperidino-3-pyridyl
O	propyl	OCOOMe	6-piperidino-3-pyridyl
O	propyl	OCOOMe	2-morpholino-3-pyridyl
O	propyl	OCOOMe	4-morpholino-3-pyridyl
O	propyl	OCOOMe	5-morpholino-3-pyridyl
O	propyl	OCOOMe	6-morpholino-3-pyridyl
O	propyl	OCOOMe	2-hydroxy-3-pyridyl
O	propyl	OCOOMe	4-hydroxy-3-pyridyl
O	propyl	OCOOMe	5-hydroxy-3-pyridyl
O	propyl	OCOOMe	6-hydroxy-3-pyridyl
O	propyl	OCOOMe	2-mercapto-3-pyridyl
O	propyl	OCOOMe	4-mercapto-3-pyridyl
O	propyl	OCOOMe	5-mercapto-3-pyridyl
O	propyl	OCOOMe	6-mercapto-3-pyridyl
O	propyl	OCOOMe	2-methylthio-3-pyridyl
O	propyl	OCOOMe	4-methylthio-3-pyridyl
O	propyl	OCOOMe	5-methylthio-3-pyridyl
O	propyl	OCOOMe	6-methylthio-3-pyridyl
O	propyl	OCOOMe	2,6-dimethyl-3-pyridyl
O	propyl	OCOOMe	5,6-dimethyl-3-pyridyl
O	propyl	OCOOMe	2,6-diethyl-3-pyridyl
O	propyl	OCOOMe	5,6-diethyl-3-pyridyl
O	propyl	OCOOMe	2,6-dimethoxy-3-pyridyl
O	propyl	OCOOMe	5,6-dimethoxy-3-pyridyl
O	propyl	OCOOMe	2,6-diethoxy-3-pyridyl
O	propyl	OCOOMe	5,6-diethoxy-3-pyridyl
O	propyl	OCOOMe	2,6-dichloro-3-pyridyl
O	propyl	OCOOMe	5,6-dichloro-3-pyridyl
O	propyl	OCOOMe	5-chloro-6-methoxy-3-pyridyl
O	propyl	OCOOMe	5-chloro-6-ethoxy-3-pyridyl
O	propyl	OCOOMe	2-chloro-6-methyl-3-pyridyl
O	propyl	OCOOMe	6-chloro-2-methyl-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	propyl	OCOOMe	2-methyl-4-pyridyl
O	propyl	OCOOMe	2-ethyl-4-pyridyl
O	propyl	OCOOMe	2-methoxy-4-pyridyl
O	propyl	OCOOMe	2-ethoxy-4-pyridyl
O	propyl	OCOOMe	2-chloro-4-pyridyl
O	propyl	OCOOMe	2-dimethylamino-4-pyridyl
O	propyl	OCOOMe	2-(1-pyrrolidinyl)-4-pyridyl
O	propyl	OCOOMe	2-piperidino-4-pyridyl
O	propyl	OCOOMe	2-morpholino-4-pyridyl
O	propyl	OCOOMe	2-methylthio-4-pyridyl
O	propyl	OCOOMe	2-pyrazinyl
O	propyl	OCOOMe	5-methyl-2-pyrazinyl
O	propyl	OCOOMe	5-ethyl-2-pyrazinyl
O	propyl	OCOOMe	5-methoxy-2-pyrazinyl
O	propyl	OCOOMe	5-ethoxy-2-pyrazinyl
O	propyl	OCOOMe	5-chloro-2-pyrazinyl
O	propyl	OCOOMe	6-methyl-2-pyrazinyl
O	propyl	OCOOMe	6-methoxy-2-pyrazinyl
O	propyl	OCOOMe	6-chloro-2-pyrazinyl
O	propyl	OCOOEt	2-pyridyl
O	propyl	OCOOEt	3-pyridyl
O	propyl	OCOOEt	4-pyridyl
O	propyl	OCOOEt	2-methyl-3-pyridyl
O	propyl	OCOOEt	4-methyl-3-pyridyl
O	propyl	OCOOEt	5-methyl-3-pyridyl
O	propyl	OCOOEt	6-methyl-3-pyridyl
O	propyl	OCOOEt	2-ethyl-3-pyridyl
O	propyl	OCOOEt	4-ethyl-3-pyridyl
O	propyl	OCOOEt	5-ethyl-3-pyridyl
O	propyl	OCOOEt	6-ethyl-3-pyridyl
O	propyl	OCOOEt	2-methoxy-3-pyridyl
O	propyl	OCOOEt	4-methoxy-3-pyridyl
O	propyl	OCOOEt	5-methoxy-3-pyridyl
O	propyl	OCOOEt	6-methoxy-3-pyridyl
O	propyl	OCOOEt	2-ethoxy-3-pyridyl
O	propyl	OCOOEt	4-ethoxy-3-pyridyl
O	propyl	OCOOEt	5-ethoxy-3-pyridyl
O	propyl	OCOOEt	6-ethoxy-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	propyl	OCOOEt	2-chloro-3-pyridyl
O	propyl	OCOOEt	4-chloro-3-pyridyl
O	propyl	OCOOEt	5-chloro-3-pyridyl
O	propyl	OCOOEt	6-chloro-3-pyridyl
O	propyl	OCOOEt	2-fluoro-3-pyridyl
O	propyl	OCOOEt	4-fluoro-3-pyridyl
O	propyl	OCOOEt	5-fluoro-3-pyridyl
O	propyl	OCOOEt	6-fluoro-3-pyridyl
O	propyl	OCOOEt	2-dimethylamino-3-pyridyl
O	propyl	OCOOEt	4-dimethylamino-3-pyridyl
O	propyl	OCOOEt	5-dimethylamino-3-pyridyl
O	. propyl	OCOOEt	6-dimethylamino-3-pyridyl
O	propyl	OCOOEt	2-(1-pyrrolidinyl)-3-pyridyl
O	propyl	OCOOEt	3-(1-pyrrolidinyl)-3-pyridyl
O	propyl	OCOOEt	5-(1-pyrrolidinyl)-3-pyridyl
O	propyl	OCOOEt	6-(1-pyrrolidinyl)-3-pyridyl
O	propyl	OCOOEt	2-piperidino-3-pyridyl
O	propyl	OCOOEt	4-piperidino-3-pyridyl
O	propyl	OCOOEt	5-piperidino-3-pyridyl
O	propyl	OCOOEt	6-piperidino-3-pyridyl
O	propyl	OCOOEt	2-morpholino-3-pyridyl
O	propyl	OCOOEt	4-morpholino-3-pyridyl
O	propyl	OCOOEt	5-morpholino-3-pyridyl
O	propyl	OCOOEt	6-morpholino-3-pyridyl
O	propyl	OCOOEt	2-hydroxy-3-pyridyl
O	propyl	OCOOEt	4-hydroxy-3-pyridyl
O	propyl	OCOOEt	5-hydroxy-3-pyridyl
O	propyl	OCOOEt	6-hydroxy-3-pyridyl
O	propyl	OCOOEt	2-mercapto-3-pyridyl
O	propyl	OCOOEt	4-mercapto-3-pyridyl
O	propyl	OCOOEt	5-mercapto-3-pyridyl
O	propyl	OCOOEt	6-mercapto-3-pyridyl
O	propyl	OCOOEt	2-methylthio-3-pyridyl
O	propyl	OCOOEt	4-methylthio-3-pyridyl
O	propyl	OCOOEt	5-methylthio-3-pyridyl
O	propyl	OCOOEt	6-methylthio-3-pyridyl
O	propyl	OCOOEt	2,6-dimethyl-3-pyridyl
O	propyl	OCOOEt	5,6-dimethyl-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	propyl	OCOOEt	2,6-diethyl-3-pyridyl
O	propyl	OCOOEt	5,6-diethyl-3-pyridyl
O	propyl	OCOOEt	2,6-dimethoxy-3-pyridyl
O	propyl	OCOOEt	5,6-dimethoxy-3-pyridyl
O	propyl	OCOOEt	2,6-diethoxy-3-pyridyl
O	propyl	OCOOEt	5,6-diethoxy-3-pyridyl
O	propyl	OCOOEt	2,6-dichloro-3-pyridyl
O	propyl	OCOOEt	5,6-dichloro-3-pyridyl
O	propyl	OCOOEt	5-chloro-6-methoxy-3-pyridyl
O	propyl	OCOOEt	5-chloro-6-ethoxy-3-pyridyl
O	propyl	OCOOEt	2-chloro-6-methyl-3-pyridyl
O	propyl	OCOOEt	6-chloro-2-methyl-3-pyridyl
O	propyl	OCOOEt	2-methyl-4-pyridyl
O	propyl	OCOOEt	2-ethyl-4-pyridyl
O	propyl	OCOOEt	2-methoxy-4-pyridyl
O	propyl	OCOOEt	2-ethoxy-4-pyridyl
O	propyl	OCOOEt	2-chloro-4-pyridyl
O	propyl	OCOOEt	2-dimethylamino-4-pyridyl
O	propyl	OCOOEt	2-(1-pyrrolidinyl)-4-pyridyl
O	propyl	OCOOEt	2-piperidino-4-pyridyl
O	propyl	OCOOEt	2-morpholino-4-pyridyl
O	propyl	OCOOEt	2-methylthio-4-pyridyl
O	propyl	OCOOEt	2-pyrazinyl
O	propyl	OCOOEt	5-methyl-2-pyrazinyl
O	propyl	OCOOEt	5-ethyl-2-pyrazinyl
O	propyl	OCOOEt	5-methoxy-2-pyrazinyl
O	propyl	OCOOEt	5-ethoxy-2-pyrazinyl
O	propyl	OCOOEt	5-chloro-2-pyrazinyl
O	propyl	OCOOEt	6-methyl-2-pyrazinyl
O	propyl	OCOOEt	6-methoxy-2-pyrazinyl
O	propyl	OCOOEt	6-chloro-2-pyrazinyl
O	n-butyl	OH	2-pyridyl
O	n-butyl	OH	3-pyridyl
O	n-butyl	OH	4-pyridyl
O	n-butyl	OH	2-methyl-3-pyridyl
O	n-butyl	OH	4-methyl-3-pyridyl
O	n-butyl	OH	5-methyl-3-pyridyl
O	n-butyl	OH	6-methyl-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-butyl	OH	2-ethyl-3-pyridyl
O	n-butyl	OH	4-ethyl-3-pyridyl
O	n-butyl	OH	5-ethyl-3-pyridyl
O	n-butyl	OH	6-ethyl-3-pyridyl
O	n-butyl	OH	2-methoxy-3-pyridyl
O	n-butyl	OH	4-methoxy-3-pyridyl
O	n-butyl	OH	5-methoxy-3-pyridyl
O	n-butyl	OH	6-methoxy-3-pyridyl
O	n-butyl	OH	2-ethoxy-3-pyridyl
O	n-butyl	OH	4-ethoxy-3-pyridyl
O	n-butyl	OH	5-ethoxy-8-pyridyl
O	n-butyl	OH	6-ethoxy-3-pyridyl
O	n-butyl	OH	2-chloro-3-pyridyl
O	n-butyl	OH	4-chloro-3-pyridyl
O	n-butyl	OH	5-chloro-3-pyridyl
O	n-butyl	OH	6-chloro-3-pyridyl
O	n-butyl	OH	2-fluoro-3-pyridyl
O	n-butyl	OH	4-fluoro-3-pyridyl
O	n-butyl	OH	5-fluoro-3-pyridyl
O	n-butyl	OH	6-fluoro-3-pyridyl
O	n-butyl	OH	2-dimethylamino-8-pyridyl
O	n-butyl	OH	4-dimethylamino-3-pyridyl
O	n-butyl	OH	5-dimethylamino-3-pyridyl
O	n-butyl	OH	6-dimethylamino-3-pyridyl
O	n-butyl	OH	2-(1-pyrrolidinyl)-3-pyridyl
O	n-butyl	OH	3-(1-pyrrolidinyl)-3-pyridyl
O	n-butyl	OH	5-(1-pyrrolidinyl)-3-pyridyl
O	n-butyl	OH	6-(1-pyrrolidinyl)-3-pyridyl
O	n-butyl	OH	2-piperidino-3-pyridyl
O	n-butyl	OH	4-piperidino-3-pyridyl
O	n-butyl	OH	5-piperidino-3-pyridyl
O	n-butyl	OH	6-piperidino-3-pyridyl
O	n-butyl	OH	2-morpholino-3-pyridyl
O	n-butyl	OH	4-morpholino-3-pyridyl
O	n-butyl	OH	5-morpholino-3-pyridyl
O	n-butyl	OH	6-morpholino-3-pyridyl
O	n-butyl	OH	2-hydroxy-3-pyridyl
O	n-butyl	OH	4-hydroxy-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-butyl	OH	5-hydroxy-3-pyridyl
O	n-butyl	OH	6-hydroxy-3-pyridyl
O	n-butyl	OH	2-mercapto-3-pyridyl
O	n-butyl	OH	4-mercapto-3-pyridyl
O	n-butyl	OH	5-mercapto-3-pyridyl
O	n-butyl	OH	6-mercapto-3-pyridyl
O	n-butyl	OH	2-methylthio-3-pyridyl
O	n-butyl	OH	4-methylthio-3-pyridyl
O	n-butyl	OH	5-methylthio-3-pyridyl
O	n-butyl	OH	6-methylthio-3-pyridyl
O	n-butyl	OH	2,6-dimethyl-3-pyridyl
O	n-butyl	OH	5,6-dimethyl-3-pyridyl
O	n-butyl	OH	2,6-diethyl-3-pyridyl
O	n-butyl	OH	5,6-diethyl-3-pyridyl
O	n-butyl	OH	2,6-dimethoxy-3-pyridyl
O	n-butyl	OH	5,6-dimethoxy-3-pyridyl
O	n-butyl	OH	2,6-diethoxy-3-pyridyl
O	n-butyl	OH	5,6-diethoxy-3-pyridyl
O	n-butyl	OH	2,6-dichloro-3-pyridyl
O	n-butyl	OH	5,6-dichloro-3-pyridyl
O	n-butyl	OH	5-chloro-6-methoxy-3-pyridyl
O	n-butyl	OH	5-chloro-6-ethoxy-3-pyridyl
O	n-butyl	OH	2-chloro-6-methyl-3-pyridyl
O	n-butyl	OH	6-chloro-2-methyl-3-pyridyl
O	n-butyl	OH	2-methyl-4-pyridyl
O	n-butyl	OH	2-ethyl-4-pyridyl
O	n-butyl	OH	2-methoxy-4-pyridyl
O	n-butyl	OH	2-ethoxy-4-pyridyl
O	n-butyl	OH	2-chloro-4-pyridyl
O	n-butyl	OH	2-dimethylamino-4-pyridyl
O	n-butyl	OH	2-(1-pyrrolidinyl)-4-pyridyl
O	n-butyl	OH	2-piperidino-4-pyridyl
O	n-butyl	OH	2-morpholino-4-pyridyl
O	n-butyl	OH	2-methylthio-4-pyridyl
O	n-butyl	OH	2-pyrazinyl
O	n-butyl	OH	5-methyl-2-pyrazinyl
O	n-butyl	OH	5-ethyl-2-pyrazinyl
O	n-butyl	OH	5-methoxy-2-pyrazinyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-butyl	OH	5-ethoxy-2-pyrazinyl
O	n-butyl	OH	5-chloro-2-pyrazinyl
O	n-butyl	OH	6-methyl-2-pyrazinyl
O	n-butyl	OH	6-methoxy-2-pyrazinyl
O	n-butyl	OH	6-chloro-2-pyrazinyl
O	n-butyl	OCOOMe	2-pyridyl
O	n-butyl	OCOOMe	3-pyridyl
O	n-butyl	OCOOMe	4-pyridyl
O	n-butyl	OCOOMe	2-methyl-3-pyridyl
O	n-butyl	OCOOMe	4-methyl-3-pyridyl
O	n-butyl	OCOOMe	5-methyl-3-pyridyl
O	n-butyl	OCOOMe	6-methyl-3-pyridyl
O	n-butyl	OCOOMe	2-ethyl-3-pyridyl
O	n-butyl	OCOOMe	4-ethyl-3-pyridyl
O	n-butyl	OCOOMe	5-ethyl-3-pyridyl
O	n-butyl	OCOOMe	6-ethyl-3-pyridyl
O	n-butyl	OCOOMe	2-methoxy-3-pyridyl
O	n-butyl	OCOOMe	4-methoxy-3-pyridyl
O	n-butyl	OCOOMe	5-methoxy-3-pyridyl
O	n-butyl	OCOOMe	6-methoxy-3-pyridyl
O	n-butyl	OCOOMe	2-ethoxy-3-pyridyl
O	n-butyl	OCOOMe	4-ethoxy-3-pyridyl
O	n-butyl	OCOOMe	5-ethoxy-3-pyridyl
O	n-butyl	OCOOMe	6-ethoxy-3-pyridyl
O	n-butyl	OCOOMe	2-chloro-3-pyridyl
O	n-butyl	OCOOMe	4-chloro-3-pyridyl
O	n-butyl	OCOOMe	5-chloro-3-pyridyl
O	n-butyl	OCOOMe	6-chloro-3-pyridyl
O	n-butyl	OCOOMe	2-fluoro-3-pyridyl
O	n-butyl	OCOOMe	4-fluoro-3-pyridyl
O	n-butyl	OCOOMe	5-fluoro-3-pyridyl
O	n-butyl	OCOOMe	6-fluoro-3-pyridyl
O	n-butyl	OCOOMe	2-dimethylamino-3-pyridyl
O	n-butyl	OCOOMe	4-dimethylamino-3-pyridyl
O	n-butyl	OCOOMe	5-dimethylamino-3-pyridyl
O	n-butyl	OCOOMe	6-dimethylamino-3-pyridyl
O	n-butyl	OCOOMe	2-(1-pyrrolidinyl)-3-pyridyl
O	n-butyl	OCOOMe	3-(1-pyrrolidinyl)-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-butyl	OCOOMe	5-(1-pyrrolidinyl)-3-pyridyl
O	n-butyl	OCOOMe	6-(1-pyrrolidinyl)-3-pyridyl
O	n-butyl	OCOOMe	2-piperidino-3-pyridyl
O	n-butyl	OCOOMe	4-piperidino-3-pyridyl
O	n-butyl	OCOOMe	5-piperidino-3-pyridyl
O	n-butyl	OCOOMe	6-piperidino-3-pyridyl
O	n-butyl	OCOOMe	2-morpholino-3-pyridyl
O	n-butyl	OCOOMe	4-morpholino-3-pyridyl
O	n-butyl	OCOOMe	5-morpholino-3-pyridyl
O	n-butyl	OCOOMe	6-morpholino-3-pyridyl
O	n-butyl	OCOOMe	2-hydroxy-3-pyridyl
O	n-butyl	OCOOMe	4-hydroxy-3-pyridyl
O	n-butyl	OCOOMe	5-hydroxy-3-pyridyl
O	n-butyl	OCOOMe	6-hydroxy-3-pyridyl
O	n-butyl	OCOOMe	2-mercapto-3-pyridyl
O	n-butyl	OCOOMe	4-mercapto-3-pyridyl
O	n-butyl	OCOOMe	5-mercapto-3-pyridyl
O	n-butyl	OCOOMe	6-mercapto-3-pyridyl
O	n-butyl	OCOOMe	2-methylthio-3-pyridyl
O	n-butyl	OCOOMe	4-methylthio-3-pyridyl
O	n-butyl	OCOOMe	5-methylthio-3-pyridyl
O	n-butyl	OCOOMe	6-methylthio-3-pyridyl
O	n-butyl	OCOOMe	2,6-dimethyl-3-pyridyl
O	n-butyl	OCOOMe	5,6-dimethyl-3-pyridyl
O	n-butyl	OCOOMe	2,6-diethyl-3-pyridyl
O	n-butyl	OCOOMe	5,6-diethyl-3-pyridyl
O	n-butyl	OCOOMe	2,6-dimethoxy-3-pyridyl
O	n-butyl	OCOOMe	5,6-dimethoxy-3-pyridyl
O	n-butyl	OCOOMe	2,6-diethoxy-3-pyridyl
O	n-butyl	OCOOMe	5,6-diethoxy-3-pyridyl
O	n-butyl	OCOOMe	2,6-dichloro-3-pyridyl
O	n-butyl	OCOOMe	5,6-dichloro-3-pyridyl
O	n-butyl	OCOOMe	5-chloro-6-methoxy-3-pyridyl
O	n-butyl	OCOOMe	5-chloro-6-ethoxy-3-pyridyl
O	n-butyl	OCOOMe	2-chloro-6-methyl-3-pyridyl
O	n-butyl	OCOOMe	6-chloro-2-methyl-3-pyridyl
O	n-butyl	OCOOMe	2-methyl-4-pyridyl
O	n-butyl	OCOOMe	2-ethyl-4-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-butyl	OCOOMe	2-methoxy-4-pyridyl
O	n-butyl	OCOOMe	2-ethoxy-4-pyridyl
O	n-butyl	OCOOMe	2-chloro-4-pyridyl
O	n-butyl	OCOOMe	2-dimethylamino-4-pyridyl
O	n-butyl	OCOOMe	2-(1-pyrrolidinyl)-4-pyridyl
O	n-butyl	OCOOMe	2-piperidino-4-pyridyl
O	n-butyl	OCOOMe	2-morpholino-4-pyridyl
O	n-butyl	OCOOMe	2-methylthio-4-pyridyl
O	n-butyl	OCOOMe	2-pyrazinyl
O	n-butyl	OCOOMe	5-methyl-2-pyrazinyl
O	n-butyl	OCOOMe	5-ethyl-2-pyrazinyl
O	n-butyl	OCOOMe	5-methoxy-2-pyrazinyl
O	n-butyl	OCOOMe	5-ethoxy-2-pyrazinyl
O	n-butyl	OCOOMe	5-chloro-2-pyrazinyl
O	n-butyl	OCOOMe	6-methyl-2-pyrazinyl
O	n-butyl	OCOOMe	6-methoxy-2-pyrazinyl
O	n-butyl	OCOOMe	6-chloro-2-pyrazinyl
O	n-butyl	OCOOEt	2-pyridyl
O	n-butyl	OCOOEt	3-pyridyl
O	n-butyl	OCOOEt	4-pyridyl
O	n-butyl	OCOOEt	2-methyl-3-pyridyl
O	n-butyl	OCOOEt	4-methyl-3-pyridyl
O	n-butyl	OCOOEt	5-methyl-3-pyridyl
O	n-butyl	OCOOEt	6-methyl-3-pyridyl
O	n-butyl	OCOOEt	2-ethyl-3-pyridyl
O	n-butyl	OCOOEt	4-ethyl-3-pyridyl
O	n-butyl	OCOOEt	5-ethyl-3-pyridyl
O	n-butyl	OCOOEt	6-ethyl-3-pyridyl
O	n-butyl	OCOOEt	2-methoxy-3-pyridyl
O	n-butyl	OCOOEt	4-methoxy-3-pyridyl
O	n-butyl	OCOOEt	5-methoxy-3-pyridyl
O	n-butyl	OCOOEt	6-methoxy-3-pyridyl
O	n-butyl	OCOOEt	2-ethoxy-3-pyridyl
O	n-butyl	OCOOEt	4-ethoxy-3-pyridyl
O	n-butyl	OCOOEt	5-ethoxy-3-pyridyl
O	n-butyl	OCOOEt	6-ethoxy-3-pyridyl
O	n-butyl	OCOOEt	2-chloro-3-pyridyl
O	n-butyl	OCOOEt	4-chloro-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-butyl	OCOOEt	5-chloro-3-pyridyl
O	n-butyl	OCOOEt	6-chloro-3-pyridyl
O	n-butyl	OCOOEt	2-fluoro-3-pyridyl
O	n-butyl	OCOOEt	4-fluoro-3-pyridyl
O	n-butyl	OCOOEt	5-fluoro-3-pyridyl
O	n-butyl	OCOOEt	6-fluoro-3-pyridyl
O	n-butyl	OCOOEt	2-dimethylamino-3-pyridyl
O	n-butyl	OCOOEt	4-dimethylamino-3-pyridyl
O	n-butyl	OCOOEt	5-dimethylamino-3-pyridyl
O	n-butyl	OCOOEt	6-dimethylamino-3-pyridyl
O	n-butyl	OCOOEt	2-(1-pyrrolidinyl)-3-pyridyl
O	n-butyl	OCOOEt	3-(1-pyrrolidinyl)-3-pyridyl
O	n-butyl	OCOOEt	5-(1-pyrrolidinyl)-3-pyridyl
O	n-butyl	OCOOEt	6-(1-pyrrolidinyl)-3-pyridyl
O	n-butyl	OCOOEt	2-piperidino-3-pyridyl
O	n-butyl	OCOOEt	4-piperidino-3-pyridyl
O	n-butyl	OCOOEt	5-piperidino-3-pyridyl
O	n-butyl	OCOOEt	6-piperidino-3-pyridyl
O	n-butyl	OCOOEt	2-morpholino-3-pyridyl
O	n-butyl	OCOOEt	4-morpholino-3-pyridyl
O	n-butyl	OCOOEt	5-morpholino-3-pyridyl
O	n-butyl	OCOOEt	6-morpholino-3-pyridyl
O	n-butyl	OCOOEt	2-hydroxy-3-pyridyl
O	n-butyl	OCOOEt	4-hydroxy-3-pyridyl
O	n-butyl	OCOOEt	5-hydroxy-3-pyridyl
O	n-butyl	OCOOEt	6-hydroxy-3-pyridyl
O	n-butyl	OCOOEt	2-mercapto-3-pyridyl
O	n-butyl	OCOOEt	4-mercapto-3-pyridyl
O	n-butyl	OCOOEt	5-mercapto-3-pyridyl
O	n-butyl	OCOOEt	6-mercapto-3-pyridyl
O	n-butyl	OCOOEt	2-methylthio-3-pyridyl
O	n-butyl	OCOOEt	4-methylthio-3-pyridyl
O	n-butyl	OCOOEt	5-methylthio-3-pyridyl
O	n-butyl	OCOOEt	6-methylthio-3-pyridyl
O	n-butyl	OCOOEt	2,6-dimethyl-3-pyridyl
O	n-butyl	OCOOEt	5,6-dimethyl-3-pyridyl
O	n-butyl	OCOOEt	2,6-diethyl-3-pyridyl
O	n-butyl	OCOOEt	5,6-diethyl-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-butyl	OCOOEt	2,6-dimethoxy-3-pyridyl
O	n-butyl	OCOOEt	5,6-dimethoxy-3-pyridyl
O	n-butyl	OCOOEt	2,6-diethoxy-3-pyridyl
O	n-butyl	OCOOEt	5,6-diethoxy-3-pyridyl
O	n-butyl	OCOOEt	2,6-dichloro-3-pyridyl
O	n-butyl	OCOOEt	5,6-dichloro-3-pyridyl
O	n-butyl	OCOOEt	5-chloro-6-methoxy-3-pyridyl
O	n-butyl	OCOOEt	5-chloro-6-ethoxy-3-pyridyl
O	n-butyl	OCOOEt	2-chloro-6-methyl-3-pyridyl
O	n-butyl	OCOOEt	6-chloro-2-methyl-3-pyridyl
O	n-butyl	OCOOEt	2-methyl-4-pyridyl
O	n-butyl	OCOOEt	2-ethyl-4-pyridyl
O	n-butyl	OCOOEt	2-methoxy-4-pyridyl
O	n-butyl	OCOOEt	2-ethoxy-4-pyridyl
O	n-butyl	OCOOEt	2-chloro-4-pyridyl
O	n-butyl	OCOOEt	2-dimethylamino-4-pyridyl
O	n-butyl	OCOOEt	2-(1-pyrrolidinyl)-4-pyridyl
O	n-butyl	OCOOEt	2-piperidino-4-pyridyl
O	n-butyl	OCOOEt	2-morpholino-4-pyridyl
O	n-butyl	OCOOEt	2-methylthio-4-pyridyl
O	n-butyl	OCOOEt	2-pyrazinyl
O	n-butyl	OCOOEt	5-methyl-2-pyrazinyl
O	n-butyl	OCOOEt	5-ethyl-2-pyrazinyl
O	n-butyl	OCOOEt	5-methoxy-2-pyrazinyl
O	n-butyl	OCOOEt	5-ethoxy-2-pyrazinyl
O	n-butyl	OCOOEt	5-chloro-2-pyrazinyl
O	n-butyl	OCOOEt	6-methyl-2-pyrazinyl
O	n-butyl	OCOOEt	6-methoxy-2-pyrazinyl
O	n-butyl	OCOOEt	6-chloro-2-pyrazinyl
O	n-pentyl	OH	2-pyridyl
O	n-pentyl	OH	3-pyridyl
O	n-pentyl	OH	4-pyridyl
O	n-pentyl	OH	2-methyl-3-pyridyl
O	n-pentyl	OH	4-methyl-3-pyridyl
O	n-pentyl	OH	5-methyl-3-pyridyl
O	n-pentyl	OH	6-methyl-3-pyridyl
O	n-pentyl	OH	2-ethyl-3-pyridyl
O	n-pentyl	OH	4-ethyl-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-pentyl	OH	5-ethyl-3-pyridyl
O	n-pentyl	OH	6-ethyl-3-pyridyl
O	n-pentyl	OH	2-methoxy-3-pyridyl
O	n-pentyl	OH	4-methoxy-3-pyridyl
O	n-pentyl	OH	5-methoxy-3-pyridyl
O	n-pentyl	OH	6-methoxy-3-pyridyl
O	n-pentyl	OH	2-ethoxy-3-pyridyl
O	n-pentyl	OH	4-ethoxy-3-pyridyl
O	n-pentyl	OH	5-ethoxy-3-pyridyl
O	n-pentyl	OH	6-ethoxy-3-pyridyl
O	n-pentyl	OH	2-chloro-3-pyridyl
O	n-pentyl	OH	4-chloro-3-pyridyl
O	n-pentyl	OH	5-chloro-3-pyridyl
O	n-pentyl	OH	6-chloro-3-pyridyl
O	n-pentyl	OH	2-fluoro-3-pyridyl
O	n-pentyl	OH	4-fluoro-3-pyridyl
O	n-pentyl	OH	5-fluoro-3-pyridyl
O	n-pentyl	OH	6-fluoro-3-pyridyl
O	n-pentyl	OH	2-dimethylamino-3-pyridyl
O	n-pentyl	OH	4-dimethylamino-3-pyridyl
O	n-pentyl	OH	5-dimethylamino-3-pyridyl
O	n-pentyl	OH	6-dimethylamino-3-pyridyl
O	n-pentyl	OH	2-(1-pyrrolidinyl)-3-pyridyl
O	n-pentyl	OH	3-(1-pyrrolidinyl)-3-pyridyl
O	n-pentyl	OH	5-(1-pyrrolidinyl)-3-pyridyl
O	n-pentyl	OH	6-(1-pyrrolidinyl)-3-pyridyl
O	n-pentyl	OH	2-piperidino-3-pyridyl
O	n-pentyl	OH	4-piperidino-3-pyridyl
O	n-pentyl	OH	5-piperidino-3-pyridyl
O	n-pentyl	OH	6-piperidino-3-pyridyl
O	n-pentyl	OH	2-morpholino-3-pyridyl
O	n-pentyl	OH	4-morpholino-3-pyridyl
O	n-pentyl	OH	5-morpholino-3-pyridyl
O	n-pentyl	OH	6-morpholino-3-pyridyl
O	n-pentyl	OH	2-hydroxy-3-pyridyl
O	n-pentyl	OH	4-hydroxy-3-pyridyl
O	n-pentyl	OH	5-hydroxy-3-pyridyl
O	n-pentyl	OH	6-hydroxy-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-pentyl	OH	2-mercapto-3-pyridyl
O	n-pentyl	OH	4-mercapto-3-pyridyl
O	n-pentyl	OH	5-mercapto-3-pyridyl
O	n-pentyl	OH	6-mercapto-3-pyridyl
O	n-pentyl	OH	2-methylthio-3-pyridyl
O	n-pentyl	OH	4-methylthio-3-pyridyl
O	n-pentyl	OH	5-methylthio-3-pyridyl
O	n-pentyl	OH	6-methylthio-3-pyridyl
O	n-pentyl	OH	2,6-dimethyl-3-pyridyl
O	n-pentyl	OH	5,6-dimethyl-3-pyridyl
O	n-pentyl	OH	2,6-diethyl-3-pyridyl
O	n-pentyl	OH	5,6-diethyl-3-pyridyl
O	n-pentyl	OH	2,6-dimethoxy-3-pyridyl
O	n-pentyl	OH	5,6-dimethoxy-3-pyridyl
O	n-pentyl	OH	2,6-diethoxy-3-pyridyl
O	n-pentyl	OH	5,6-diethoxy-3-pyridyl
O	n-pentyl	OH	2,6-dichloro-3-pyridyl
O	n-pentyl	OH	5,6-dichloro-3-pyridyl
O	n-pentyl	OH	5-chloro-6-methoxy-3-pyridyl
O	n-pentyl	OH	5-chloro-6-ethoxy-3-pyridyl
O	n-pentyl	OH	2-chloro-6-methyl-3-pyridyl
O	n-pentyl	OH	6-chloro-2-methyl-3-pyridyl
O	n-pentyl	OH	2-methyl-4-pyridyl
O	n-pentyl	OH	2-ethyl-4-pyridyl
O	n-pentyl	OH	2-methoxy-4-pyridyl
O	n-pentyl	OH	2-ethoxy-4-pyridyl
O	n-pentyl	OH	2-chloro-4-pyridyl
O	n-pentyl	OH	2-dimethylamino-4-pyridyl
O	n-pentyl	OH	2-(1-pyrrolidinyl)-4-pyridyl
O	n-pentyl	OH	2-piperidino-4-pyridyl
O	n-pentyl	OH	2-morpholino-4-pyridyl
O	n-pentyl	OH	2-methylthio-4-pyridyl
O	n-pentyl	OH	2-pyrazinyl
O	n-pentyl	OH	5-methyl-2-pyrazinyl
O	n-pentyl	OH	5-ethyl-2-pyrazinyl
O	n-pentyl	OH	5-methoxy-2-pyrazinyl
O	n-pentyl	OH	5-ethoxy-2-pyrazinyl
O	n-pentyl	OH	5-chloro-2-pyrazinyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-pentyl	OH	6-methyl-2-pyrazinyl
O	n-pentyl	OH	6-methoxy-2-pyrazinyl
O	n-pentyl	OH	6-chloro-2-pyrazinyl
O	n-pentyl	OCOOMe	2-pyridyl
O	n-pentyl	OCOOMe	3-pyridyl
O	n-pentyl	OCOOMe	4-pyridyl
O	n-pentyl	OCOOMe	2-methyl-3-pyridyl
O	n-pentyl	OCOOMe	4-methyl-3-pyridyl
O	n-pentyl	OCOOMe	5-methyl-3-pyridyl
O	n-pentyl	OCOOMe	6-methyl-3-pyridyl
O	n-pentyl	OCOOMe	2-ethyl-3-pyridyl
O	n-pentyl	OCOOMe	4-ethyl-3-pyridyl
O	n-pentyl	OCOOMe	5-ethyl-3-pyridyl
O	n-pentyl	OCOOMe	6-ethyl-3-pyridyl
O	n-pentyl	OCOOMe	2-methoxy-3-pyridyl
O	n-pentyl	OCOOMe	4-methoxy-3-pyridyl
O	n-pentyl	OCOOMe	5-methoxy-3-pyridyl
O	n-pentyl	OCOOMe	6-methoxy-3-pyridyl
O	n-pentyl	OCOOMe	2-ethoxy-3-pyridyl
O	n-pentyl	OCOOMe	4-ethoxy-3-pyridyl
O	n-pentyl	OCOOMe	5-ethoxy-3-pyridyl
O	n-pentyl	OCOOMe	6-ethoxy-3-pyridyl
O	n-pentyl	OCOOMe	2-chloro-3-pyridyl
O	n-pentyl	OCOOMe	4-chloro-3-pyridyl
O	n-pentyl	OCOOMe	5-chloro-3-pyridyl
O	n-pentyl	OCOOMe	6-chloro-3-pyridyl
O	n-pentyl	OCOOMe	2-fluoro-3-pyridyl
O	n-pentyl	OCOOMe	4-fluoro-3-pyridyl
O	n-pentyl	OCOOMe	5-fluoro-3-pyridyl
O	n-pentyl	OCOOMe	6-fluoro-3-pyridyl
O	n-pentyl	OCOOMe	2-dimethylamino-3-pyridyl
O	n-pentyl	OCOOMe	4-dimethylamino-3-pyridyl
O	n-pentyl	OCOOMe	5-dimethylamino-3-pyridyl
O	n-pentyl	OCOOMe	6-dimethylamino-3-pyridyl
O	n-pentyl	OCOOMe	2-(1-pyrrolidinyl)-3-pyridyl
O	n-pentyl	OCOOMe	3-(1-pyrrolidinyl)-3-pyridyl
O	n-pentyl	OCOOMe	5-(1-pyrrolidinyl)-3-pyridyl
O	n-pentyl	OCOOMe	6-(1-pyrrolidinyl)-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-pentyl	OCOOMe	2-piperidino-3-pyridyl
O	n-pentyl	OCOOMe	4-piperidino-3-pyridyl
O	n-pentyl	OCOOMe	5-piperidino-3-pyridyl
O	n-pentyl	OCOOMe	6-piperidino-3-pyridyl
O	n-pentyl	OCOOMe	2-morpholino-3-pyridyl
O	n-pentyl	OCOOMe	4-morpholino-3-pyridyl
O	n-pentyl	OCOOMe	5-morpholino-3-pyridyl
O	n-pentyl	OCOOMe	6-morpholino-3-pyridyl
O	n-pentyl	OCOOMe	2-hydroxy-3-pyridyl
O	n-pentyl	OCOOMe	4-hydroxy-3-pyridyl
O	n-pentyl	OCOOMe	5-hydroxy-3-pyridyl
O	n-pentyl	OCOOMe	6-hydroxy-3-pyridyl
O	n-pentyl	OCOOMe	2-mercapto-3-pyridyl
O	n-pentyl	OCOOMe	4-mercapto-3-pyridyl
O	n-pentyl	OCOOMe	5-mercapto-3-pyridyl
O	n-pentyl	OCOOMe	6-mercapto-3-pyridyl
O	n-pentyl	OCOOMe	2-methylthio-3-pyridyl
O	n-pentyl	OCOOMe	4-methylthio-3-pyridyl
O	n-pentyl	OCOOMe	5-methylthio-3-pyridyl
O	n-pentyl	OCOOMe	6-methylthio-3-pyridyl
O	n-pentyl	OCOOMe	2,6-dimethyl-3-pyridyl
O	n-pentyl	OCOOMe	5,6-dimethyl-3-pyridyl
O	n-pentyl	OCOOMe	2,6-diethyl-3-pyridyl
O	n-pentyl	OCOOMe	5,6-diethyl-3-pyridyl
O	n-pentyl	OCOOMe	2,6-dimethoxy-3-pyridyl
O	n-pentyl	OCOOMe	5,6-dimethoxy-3-pyridyl
O	n-pentyl	OCOOMe	2,6-diethoxy-3-pyridyl
O	n-pentyl	OCOOMe	5,6-diethoxy-3-pyridyl
O	n-pentyl	OCOOMe	2,6-dichloro-3-pyridyl
O	n-pentyl	OCOOMe	5,6-dichloro-3-pyridyl
O	n-pentyl	OCOOMe	5-chloro-6-methoxy-3-pyridyl
O	n-pentyl	OCOOMe	5-chloro-6-ethoxy-3-pyridyl
O	n-pentyl	OCOOMe	2-chloro-6-methyl-3-pyridyl
O	n-pentyl	OCOOMe	6-chloro-2-methyl-3-pyridyl
O	n-pentyl	OCOOMe	2-methyl-4-pyridyl
O	n-pentyl	OCOOMe	2-ethyl-4-pyridyl
O	n-pentyl	OCOOMe	2-methoxy-4-pyridyl
O	n-pentyl	OCOOMe	2-ethoxy-4-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-pentyl	OCOOMe	2-chloro-4-pyridyl
O	n-pentyl	OCOOMe	2-dimethylamino-4-pyridyl
O	n-pentyl	OCOOMe	2-(1-pyrrolidinyl)-4-pyridyl
O	n-pentyl	OCOOMe	2-piperidino-4-pyridyl
O	n-pentyl	OCOOMe	2-morpholino-4-pyridyl
O	n-pentyl	OCOOMe	2-methylthio-4-pyridyl
O	n-pentyl	OCOOMe	2-pyrazinyl
O	n-pentyl	OCOOMe	5-methyl-2-pyrazinyl
O	n-pentyl	OCOOMe	5-ethyl-2-pyrazinyl
O	n-pentyl	OCOOMe	5-methoxy-2-pyrazinyl
O	n-pentyl	OCOOMe	5-ethoxy-2-pyrazinyl
O	n-pentyl	OCOOMe	5-chloro-2-pyrazinyl
O	n-pentyl	OCOOMe	6-methyl-2-pyrazinyl
O	n-pentyl	OCOOMe	6-methoxy-2-pyrazinyl
O	n-pentyl	OCOOMe	6-chloro-2-pyrazinyl
O	n-pentyl	OCOOEt	2-pyridyl
O	n-pentyl	OCOOEt	3-pyridyl
O	n-pentyl	OCOOEt	4-pyridyl
O	n-pentyl	OCOOEt	2-methyl-3-pyridyl
O	n-pentyl	OCOOEt	4-methyl-3-pyridyl
O	n-pentyl	OCOOEt	5-methyl-3-pyridyl
O	n-pentyl	OCOOEt	6-methyl-3-pyridyl
O	n-pentyl	OCOOEt	2-ethyl-3-pyridyl
O	n-pentyl	OCOOEt	4-ethyl-3-pyridyl
O	n-pentyl	OCOOEt	5-ethyl-3-pyridyl
O	n-pentyl	OCOOEt	6-ethyl-3-pyridyl
O	n-pentyl	OCOOEt	2-methoxy-3-pyridyl
O	n-pentyl	OCOOEt	4-methoxy-3-pyridyl
O	n-pentyl	OCOOEt	5-methoxy-3-pyridyl
O	n-pentyl	OCOOEt	6-methoxy-3-pyridyl
O	n-pentyl	OCOOEt	2-ethoxy-3-pyridyl
O	n-pentyl	OCOOEt	4-ethoxy-3-pyridyl
O	n-pentyl	OCOOEt	5-ethoxy-3-pyridyl
O	n-pentyl	OCOOEt	6-ethoxy-3-pyridyl
O	n-pentyl	OCOOEt	2-chloro-3-pyridyl
O	n-pentyl	OCOOEt	4-chloro-3-pyridyl
O	n-pentyl	OCOOEt	5-chloro-3-pyridyl
O	n-pentyl	OCOOEt	6-chloro-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-pentyl	OCOOEt	2-fluoro-3-pyridyl
O	n-pentyl	OCOOEt	4-fluoro-3-pyridyl
O	n-pentyl	OCOOEt	5-fluoro-3-pyridyl
O	n-pentyl	OCOOEt	6-fluoro-3-pyridyl
O	n-pentyl	OCOOEt	2-dimethylamino-3-pyridyl
O	n-pentyl	OCOOEt	4-dimethylamino-3-pyridyl
O	n-pentyl	OCOOEt	5-dimethylamino-3-pyridyl
O	n-pentyl	OCOOEt	6-dimethylamino-3-pyridyl
O	n-pentyl	OCOOEt	2-(1-pyrrolidinyl)-3-pyridyl
O	n-pentyl	OCOOEt	3-(1-pyrrolidinyl)-3-pyridyl
O	n-pentyl	OCOOEt	5-(1-pyrrolidinyl)-3-pyridyl
O	n-pentyl	OCOOEt	6-(1-pyrrolidinyl)-3-pyridyl
O	n-pentyl	OCOOEt	2-piperidino-3-pyridyl
O	n-pentyl	OCOOEt	4-piperidino-3-pyridyl
O	n-pentyl	OCOOEt	5-piperidino-3-pyridyl
O	n-pentyl	OCOOEt	6-piperidino-3-pyridyl
O	n-pentyl	OCOOEt	2-morpholino-3-pyridyl
O	n-pentyl	OCOOEt	4-morpholino-3-pyridyl
O	n-pentyl	OCOOEt	5-morpholino-3-pyridyl
O	n-pentyl	OCOOEt	6-morphalino-3-pyridyl
O	n-pentyl	OCOOEt	2-hydroxy-3-pyridyl
O	n-pentyl	OCOOEt	4-hydroxy-3-pyridyl
O	n-pentyl	OCOOEt	5-hydroxy-3-pyridyl
O	n-pentyl	OCOOEt	6-hydroxy-3-pyridyl
O	n-pentyl	OCOOEt	2-mercapto-3-pyridyl
O	n-pentyl	OCOOEt	4-mercapto-3-pyridyl
O	n-pentyl	OCOOEt	5-mercapto-3-pyridyl
O	n-pentyl	OCOOEt	6-mercapto-3-pyridyl
O	n-pentyl	OCOOEt	2-methylthio-3-pyridyl
O	n-pentyl	OCOOEt	4-methylthio-3-pyridyl
O	n-pentyl	OCOOEt	5-methylthio-3-pyridyl
O	n-pentyl	OCOOEt	6-methylthio-3-pyridyl
O	n-pentyl	OCOOEt	2,6-dimethyl-3-pyridyl
O	n-pentyl	OCOOEt	5,6-dimethyl-3-pyridyl
O	n-pentyl	OCOOEt	2,6-diethyl-3-pyridyl
O	n-pentyl	OCOOEt	5,6-diethyl-3-pyridyl
O	n-pentyl	OCOOEt	2,6-dimethoxy-3-pyridyl
O	n-pentyl	OCOOEt	5,6-dimethoxy-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-pentyl	OCOOEt	2,6-diethoxy-3-pyridyl
O	n-pentyl	OCOOEt	5,6-diethoxy-3-pyridyl
O	n-pentyl	OCOOEt	2,6-dichloro-3-pyridyl
O	n-pentyl	OCOOEt	5,6-dichloro-3-pyridyl
O	n-pentyl	OCOOEt	5-chloro-6-methoxy-3-pyridyl
O	n-pentyl	OCOOEt	5-chloro-6-ethoxy-3-pyridyl
O	n-pentyl	OCOOEt	2-chloro-6-methyl-3-pyridyl
O	n-pentyl	OCOOEt	6-chloro-2-methyl-3-pyridyl
O	n-pentyl	OCOOEt	2-methyl-4-pyridyl
O	n-pentyl	OCOOEt	2-ethyl-4-pyridyl
O	n-pentyl	OCOOEt	2-methoxy-4-pyridyl
O	n-pentyl	OCOOEt	2-ethoxy-4-pyridyl
O	n-pentyl	OCOOEt	2-chloro-4-pyridyl
O	n-pentyl	OCOOEt	2-dimethylamino-4-pyridyl
O	n-pentyl	OCOOEt	2-(1-pyrrolidinyl)-4-pyridyl
O	n-pentyl	OCOOEt	2-piperidino-4-pyridyl
O	n-pentyl	OCOOEt	2-morpholino-4-pyridyl
O	n-pentyl	OCOOEt	2-methylthio-4-pyridyl
O	n-pentyl	OCOOEt	2-pyrazinyl
O	n-pentyl	OCOOEt	5-methyl-2-pyrazinyl
O	n-pentyl	OCOOEt	5-ethyl-2-pyrazinyl
O	n-pentyl	OCOOEt	5-methoxy-2-pyrazinyl
O	n-pentyl	OCOOEt	5-ethoxy-2-pyrazinyl
O	n-pentyl	OCOOEt	5-chloro-2-pyrazinyl
O	n-pentyl	OCOOEt	6-methyl-2-pyrazinyl
O	n-pentyl	OCOOEt	6-methoxy-2-pyrazinyl
O	n-pentyl	OCOOEt	6-chloro-2-pyrazinyl
S	propyl	OH	2-pyridyl
S	propyl	OH	3-pyridyl
S	propyl	OH	4-pyridyl
S	propyl	OH	2-methyl-3-pyridyl
S	propyl	OH	4-methyl-3-pyridyl
S	propyl	OH	5-methyl-3-pyridyl
S	propyl	OH	6-methyl-3-pyridyl
S	propyl	OH	2-ethyl-3-pyridyl
S	propyl	OH	4-ethyl-3-pyridyl
S	propyl	OH	5-ethyl-3-pyridyl
S	propyl	OH	6-ethyl-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	propyl	OH	2-methoxy-3-pyridyl
S	propyl	OH	4-methoxy-3-pyridyl
S	propyl	OH	5-methoxy-3-pyridyl
S	propyl	OH	6-methoxy-3-pyridyl
S	propyl	OH	2-ethoxy-3-pyridyl
S	propyl	OH	4-ethoxy-3-pyridyl
S	propyl	OH	5-ethoxy-3-pyridyl
S	propyl	OH	6-ethoxy-3-pyridyl
S	propyl	OH	2-chloro-3-pyridyl
S	propyl	OH	4-chloro-3-pyridyl
S	propyl	OH	5-chloro-3-pyridyl
S	propyl	OH	6-chloro-3-pyridyl
S	propyl	OH	2-fluoro-3-pyridyl
S	propyl	OH	4-fluoro-3-pyridyl
S	propyl	OH	5-fluoro-3-pyridyl
S	propyl	OH	6-fluoro-3-pyridyl
S	propyl	OH	2-dimethylamino-3-pyridyl
S	propyl	OH	4-dimethylamino-3-pyridyl
S	propyl	OH	5-dimethylamino-3-pyridyl
S	propyl	OH	6-dimethylamino-3-pyridyl
S	propyl	OH	2-(1-pyrrolidinyl)-3-pyridyl
S	propyl	OH	3-(1-pyrrolidinyl)-3-pyridyl
S	propyl	OH	5-(1-pyrrolidinyl)-3-pyridyl
S	propyl	OH	6-(1-pyrrolidinyl)-3-pyridyl
S	propyl	OH	2-piperidino-3-pyridyl
S	propyl	OH	4-piperidino-3-pyridyl
S	propyl	OH	5-piperidino-3-pyridyl
S	propyl	OH	6-piperidino-3-pyridyl
S	propyl	OH	2-morpholino-3-pyridyl
S	propyl	OH	4-morpholino-3-pyridyl
S	propyl	OII	5-morpholino-3-pyridyl
S	propyl	OH	6-morpholino-3-pyridyl
S	propyl	OH	2-hydroxy-3-pyridyl
S	propyl	OH	4-hydroxy-3-pyridyl
S	propyl	OH	5-hydroxy-3-pyridyl
S	propyl	OH	6-hydroxy-3-pyridyl
S	propyl	OH	2-mercapto-3-pyridyl
S	propyl	OH	4-mercapto-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	propyl	OH	5-mercapto-3-pyridyl
S	propyl	OH	6-mercapto-3-pyridyl
S	propyl	OH	2-methylthio-3-pyridyl
S	propyl	OH	4-methylthio-3-pyridyl
S	propyl	OH	5-methylthio-3-pyridyl
S	propyl	OH	6-methylthio-3-pyridyl
S	propyl	OH	2,6-dimethyl-3-pyridyl
S	propyl	OH	5,6-dimethyl-3-pyridyl
S	propyl	OH	2,6-diethyl-3-pyridyl
S	propyl	OH	5,6-diethyl-3-pyridyl
S	propyl	OH	2,6-dimethoxy-3-pyridyl
S	propyl	OH	5,6-dimethoxy-3-pyridyl
S	propyl	OH	2,6-diethoxy-3-pyridyl
S	propyl	OH	5,6-diethoxy-3-pyridyl
S	propyl	OH	2,6-dichloro-3-pyridyl
S	propyl	OH	5,6-dichloro-3-pyridyl
S	propyl	OH	5-chloro-6-methoxy-3-pyridyl
S	propyl	OH	5-chloro-6-ethoxy-3-pyridyl
S	propyl	OH	2-chloro-6-methyl-3-pyridyl
S	propyl	OH	6-chloro-2-methyl-3-pyridyl
S	propyl	OH	2-methyl-4-pyridyl
S	propyl	OH	2-ethyl-4-pyridyl
S	propyl	OH	2-methoxy-4-pyridyl
S	propyl	OH	2-ethoxy-4-pyridyl
S	propyl	OH	2-chloro-4-pyridyl
S	propyl	OH	2-dimethylamino-4-pyridyl
S	propyl	OH	2-(1-pyrrolidinyl)-4-pyridyl
S	propyl	OH	2-piperidino-4-pyridyl
S	propyl	OH	2-morpholino-4-pyridyl
S	propyl	OH	2-methylthio-4-pyridyl
S	propyl	OH	2-pyrazinyl
S	propyl	OH	5-methyl-2-pyrazinyl
S	propyl	OH	5-ethyl-2-pyrazinyl
S	propyl	OH	5-methoxy-2-pyrazinyl
S	propyl	OH	5-ethoxy-2-pyrazinyl
S	propyl	OH	5-chloro-2-pyrazinyl
S	propyl	OH	6-methyl-2-pyrazinyl
S	propyl	OH	6-methoxy-2-pyrazinyl

Table 1 (continued)

X	R^1	R^2	Y
S	propyl	OH	6-chloro-2-pyrazinyl
S	propyl	OCOOMe	2-pyridyl
S	propyl	OCOOMe	3-pyridyl
S	propyl	OCOOMe	4-pyridyl
S	propyl	OCOOMe	2-methyl-3-pyridyl
S	propyl	OCOOMe	4-methyl-3-pyridyl
S	propyl	OCOOMe	5-methyl-3-pyridyl
S	propyl	OCOOMe	6-methyl-3-pyridyl
S	propyl	OCOOMe	2-ethyl-3-pyridyl
S	propyl	OCOOMe	4-ethyl-3-pyridyl
S	propyl	OCOOMe	5-ethyl-3-pyridyl
S	propyl	OCOOMe	6-ethyl-3-pyridyl
S	propyl	OCOOMe	2-methoxy-3-pyridyl
S	propyl	OCOOMe	4-methoxy-3-pyridyl
S	propyl	OCOOMe	5-methoxy-3-pyridyl
S	propyl	OCOOMe	6-methoxy-3-pyridyl
S	propyl	OCOOMe	2-ethoxy-3-pyridyl
S	propyl	OCOOMe	4-ethoxy-3-pyridyl
S	propyl	OCOOMe	5-ethoxy-3-pyridyl
S	propyl	OCOOMe	6-ethoxy-3-pyridyl
S	propyl	OCOOMe	2-chloro-3-pyridyl
S	propyl	OCOOMe	4-chloro-3-pyridyl
S	propyl	OCOOMe	5-chloro-3-pyridyl
S	propyl	OCOOMe	6-chloro-3-pyridyl
S	propyl	OCOOMe	2-fluoro-3-pyridyl
S	propyl	OCOOMe	4-fluoro-3-pyridyl
S	propyl	OCOOMe	5-fluoro-3-pyridyl
S	propyl	OCOOMe	6-fluoro-3-pyridyl
S	propyl	OCOOMe	2-dimethylamino-3-pyridyl
S	propyl	OCOOMe	4-dimethylamino-3-pyridyl
S	propyl	OCOOMe	5-dimethylamino-3-pyridyl
S	propyl	OCOOMe	6-dimethylamino-3-pyridyl
S	propyl	OCOOMe	2-(1-pyrrolidinyl)-3-pyridyl
S	propyl	OCOOMe	3-(1-pyrrolidinyl)-3-pyridyl
S	propyl	OCOOMe	5-(1-pyrrolidinyl)-3-pyridyl
S	propyl	OCOOMe	6-(1-pyrrolidinyl)-3-pyridyl
S	propyl	OCOOMe	2-piperidino-3-pyridyl
S	propyl	OCOOMe	4-piperidino-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	propyl	OCOOMe	5-piperidino-3-pyridyl
S	propyl	OCOOMe	6-piperidino-3-pyridyl
S	propyl	OCOOMe	2-morpholino-3-pyridyl
S	propyl	OCOOMe	4-morpholino-3-pyridyl
S	propyl	OCOOMe	5-morpholino-3-pyridyl
S	propyl	OCOOMe	6-morpholino-3-pyridyl
S	propyl	OCOOMe	2-hydroxy-3-pyridyl
S	propyl	OCOOMe	4-hydroxy-3-pyridyl
S	propyl	OCOOMe	5-hydroxy-3-pyridyl
S	propyl	OCOOMe	6-hydroxy-3-pyridyl
S	propyl	OCOOMe	2-mercapto-3-pyridyl
S	propyl	OCOOMe	4-mercapto-3-pyridyl
S	propyl	OCOOMe	5-mercapto-3-pyridyl
S	propyl	OCOOMe	6-mercapto-3-pyridyl
S	propyl	OCOOMe	2-methylthio-3-pyridyl
S	propyl	OCOOMe	4-methylthio-3-pyridyl
S	propyl	OCOOMe	5-methylthio-3-pyridyl
S	propyl	OCOOMe	6-methylthio-3-pyridyl
S	propyl	OCOOMe	2,6-dimethyl-3-pyridyl
S	propyl	OCOOMe	5,6-dimethyl-3-pyridyl
S	propyl	OCOOMe	2,6-diethyl-3-pyridyl
S	propyl	OCOOMe	5,6-diethyl-3-pyridyl
S	propyl	OCOOMe	2,6-dimethoxy-3-pyridyl
S	propyl	OCOOMe	5,6-dimethoxy-3-pyridyl
S	propyl	OCOOMe	2,6-diethoxy-3-pyridyl
S	propyl	OCOOMe	5,6-diethoxy-3-pyridyl
S	propyl	OCOOMe	2,6-dichloro-3-pyridyl
S	propyl	OCOOMe	5,6-dichloro-3-pyridyl
S	propyl	OCOOMe	5-chloro-6-methoxy-3-pyridyl
S	propyl	OCOOMe	5-chloro-6-ethoxy-3-pyridyl
S	propyl	OCOOMe	2-chloro-6-methyl-3-pyridyl
S	propyl	OCOOMe	6-chloro-2-methyl-3-pyridyl
S	propyl	OCOOMe	2-methyl-4-pyridyl
S	propyl	OCOOMe	2-ethyl-4-pyridyl
S	propyl	OCOOMe	2-methoxy-4-pyridyl
S	propyl	OCOOMe	2-ethoxy-4-pyridyl
S	propyl	OCOOMe	2-chloro-4-pyridyl
S	propyl	OCOOMe	2-dimethylamino-4-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	propyl	OCOOMe	2-(1-pyrrolidinyl)-4-pyridyl
S	propyl	OCOOMe	2-piperidino-4-pyridyl
S	propyl	OCOOMe	2-morpholino-4-pyridyl
S	propyl	OCOOMe	2-methylthio-4-pyridyl
S	propyl	OCOOMe	2-pyrazinyl
S	propyl	OCOOMe	5-methyl-2-pyrazinyl
S	propyl	OCOOMe	5-ethyl-2-pyrazinyl
S	propyl	OCOOMe	5-methoxy-2-pyrazinyl
S	propyl	OCOOMe	5-ethoxy-2-pyrazinyl
S	propyl	OCOOMe	5-chloro-2-pyrazinyl
S	propyl	OCOOMe	6-methyl-2-pyrazinyl
S	propyl	OCOOMe	6-methoxy-2-pyrazinyl
S	propyl	OCOOMe	6-chloro-2-pyrazinyl
S	propyl	OCOOEt	2-pyridyl
S	propyl	OCOOEt	3-pyridyl
S	propyl	OCOOEt	4-pyridyl
S	propyl	OCOOEt	2-methyl-3-pyridyl
S	propyl	OCOOEt	4-methyl-3-pyridyl
S	propyl	OCOOEt	5-methyl-3-pyridyl
S	propyl	OCOOEt	6-methyl-3-pyridyl
S	propyl	OCOOEt	2-ethyl-3-pyridyl
S	propyl	OCOOEt	4-ethyl-3-pyridyl
S	propyl	OCOOEt	5-ethyl-3-pyridyl
S	propyl	OCOOEt	6-ethyl-3-pyridyl
S	propyl	OCOOEt	2-methoxy-3-pyridyl
S	propyl	OCOOEt	4-methoxy-3-pyridyl
S	propyl	OCOOEt	5-methoxy-3-pyridyl
S	propyl	OCOOEt	6-methoxy-3-pyridyl
S	propyl	OCOOEt	2-ethoxy-3-pyridyl
S	propyl	OCOOEt	4-ethoxy-3-pyridyl
S	propyl	OCOOEt	5-ethoxy-3-pyridyl
S	propyl	OCOOEt	6-ethoxy-3-pyridyl
S	propyl	OCOOEt	2-chloro-3-pyridyl
S	propyl	OCOOEt	4-chloro-3-pyridyl
S	propyl	OCOOEt	5-chloro-3-pyridyl
S	propyl	OCOOEt	6-chloro-3-pyridyl
S	propyl	OCOOEt	2-fluoro-3-pyridyl
S	propyl	OCOOEt	4-fluoro-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	propyl	OCOOEt	5-fluoro-3-pyridyl
S	propyl	OCOOEt	6-fluoro-3-pyridyl
S	propyl	OCOOEt	2-dimethylamino-3-pyridyl
S	propyl	OCOOEt	4-dimethylamino-3-pyridyl
S	propyl	OCOOEt	5-dimethylamino-3-pyridyl
S	propyl	OCOOEt	6-dimethylamino-3-pyridyl
S	propyl	OCOOEt	2-(1-pyrrolidinyl)-3-pyridyl
S	propyl	OCOOEt	3-(1-pyrrolidinyl)-3-pyridyl
S	propyl	OCOOEt	5-(1-pyrrolidinyl)-3-pyridyl
S	propyl	OCOOEt	6-(1-pyrrolidinyl)-3-pyridyl
S	propyl	OCOOEt	2-piperidino-3-pyridyl
S	propyl	OCOOEt	4-piperidino-3-pyridyl
S	propyl	OCOOEt	5-piperidino-3-pyridyl
S	propyl	OCOOEt	6-piperidino-3-pyridyl
S	propyl	OCOOEt	2-morpholino-3-pyridyl
S	propyl	OCOOEt	4-morpholino-3-pyridyl
S	propyl	OCOOEt	5-morpholino-3-pyridyl
S	propyl	OCOOEt	6-morpholino-3-pyridyl
S	propyl	OCOOEt	2-hydroxy-3-pyridyl
S	propyl	OCOOEt	4-hydroxy-3-pyridyl
S	propyl	OCOOEt	5-hydroxy-3-pyridyl
S	propyl	OCOOEt	6-hydroxy-3-pyridyl
S	propyl	OCOOEt	2-mercapto-3-pyridyl
S	propyl	OCOOEt	4-mercapto-3-pyridyl
S	propyl	OCOOEt	5-mercapto-3-pyridyl
S	propyl	OCOOEt	6-mercapto-3-pyridyl
S	propyl	OCOOEt	2-methylthio-3-pyridyl
S	propyl	OCOOEt	4-methylthio-3-pyridyl
S	propyl	OCOOEt	5-methylthio-3-pyridyl
S	propyl	OCOOEt	6-methylthio-3-pyridyl
S	propyl	OCOOEt	2,6-dimethyl-3-pyridyl
S	propyl	OCOOEt	5,6-dimethyl-3-pyridyl
S	propyl	OCOOEt	2,6-diethyl-3-pyridyl
S	propyl	OCOOEt	5,6-diethyl-3-pyridyl
S	propyl	OCOOEt	2,6-dimethoxy-3-pyridyl
S	propyl	OCOOEt	5,6-dimethoxy-3-pyridyl
S	propyl	OCOOEt	2,6-diethoxy-3-pyridyl
S	propyl	OCOOEt	5,6-diethoxy-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	propyl	OCOOEt	2,6-dichloro-3-pyridyl
S	propyl	OCOOEt	5,6-dichloro-3-pyridyl
S	propyl	OCOOEt	5-chloro-6-methoxy-3-pyridyl
S	propyl	OCOOEt	5-chloro-6-ethoxy-3-pyridyl
S	propyl	OCOOEt	2-chloro-6-methyl-3-pyridyl
S	propyl	OCOOEt	6-chloro-2-methyl-3-pyridyl
S	propyl	OCOOEt	2-methyl-4-pyridyl
S	propyl	OCOOEt	2-ethyl-4-pyridyl
S	propyl	OCOOEt	2-methoxy-4-pyridyl
S	propyl	OCOOEt	2-ethoxy-4-pyridyl
S	propyl	OCOOEt	2-chloro-4-pyridyl
S	propyl	OCOOEt	2-dimethylamino-4-pyridyl
S	propyl	OCOOEt	2-(1-pyrrolidinyl)-4-pyridyl
S	propyl	OCOOEt	2-piperidino-4-pyridyl
S	propyl	OCOOEt	2-morpholino-4-pyridyl
S	propyl	OCOOEt	2-methylthio-4-pyridyl
S	propyl	OCOOEt	2-pyrazinyl
S	propyl	OCOOEt	5-methyl-2-pyrazinyl
S	propyl	OCOOEt	5-ethyl-2-pyrazinyl
S	propyl	OCOOEt	5-methoxy-2-pyrazinyl
S	propyl	OCOOEt	5-ethoxy-2-pyrazinyl
S	propyl	OCOOEt	5-chloro-2-pyrazinyl
S	propyl	OCOOEt	6-methyl-2-pyrazinyl
S	propyl	OCOOEt	6-methoxy-2-pyrazinyl
S	propyl	OCOOEt	6-chloro-2-pyrazinyl
S	n-butyl	OH	2-pyridyl
S	n-butyl	OH	3-pyridyl
S	n-butyl	OH	4-pyridyl
S	n-butyl	OH	2-methyl-3-pyridyl
S	n-butyl	OH	4-methyl-3-pyridyl
S	n-butyl	OH	5-methyl-3-pyridyl
S	n-butyl	OH	6-methyl-3-pyridyl
S	n-butyl	OH	2-ethyl-3-pyridyl
S	n-butyl	OH	4-ethyl-3-pyridyl
S	n-butyl	OH	5-ethyl-3-pyridyl
S	n-butyl	OH	6-ethyl-3-pyridyl
S	n-butyl	OH	2-methoxy-3-pyridyl
S	n-butyl	OH	4-methoxy-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-butyl	OH	5-methoxy-3-pyridyl
S	n-butyl	OH	6-methoxy-3-pyridyl
S	n-butyl	OH	2-ethoxy-3-pyridyl
S	n-butyl	OH	4-ethoxy-3-pyridyl
S	n-butyl	OH	5-ethoxy-3-pyridyl
S	n-butyl	OH	6-ethoxy-3-pyridyl
S	n-butyl	OH	2-chloro-3-pyridyl
S	n-butyl	OH	4-chloro-3-pyridyl
S	n-butyl	OH	5-chloro-3-pyridyl
S	n-butyl	OH	6-chloro-3-pyridyl
S	n-butyl	OH	2-fluoro-3-pyridyl
S	n-butyl	OH	4-fluoro-3-pyridyl
S	n-butyl	OH	5-fluoro-3-pyridyl
S	n-butyl	OH	6-fluoro-3-pyridyl
S	n-butyl	OH	2-dimethylamino-3-pyridyl
S	n-butyl	OH	4-dimethylamino-3-pyridyl
S	n-butyl	OH	5-dimethylamino-3-pyridyl
S	n-butyl	OH	6-dimethylamino-3-pyridyl
S	n-butyl	OH	2-(1-pyrrolidinyl)-3-pyridyl
S	n-butyl	OH	3-(1-pyrrolidinyl)-3-pyridyl
S	n-butyl	OH	5-(1-pyrrolidinyl)-3-pyridyl
S	n-butyl	OH	6-(1-pyrrolidinyl)-3-pyridyl
S	n-butyl	OH	2-piperidino-3-pyridyl
S	n-butyl	OH	4-piperidino-3-pyridyl
S	n-butyl	OH	5-piperidino-3-pyridyl
S	n-butyl	OH	6-piperidino-3-pyridyl
S	n-butyl	OH	2-morpholino-3-pyridyl
S	n-butyl	OH	4-morpholino-3-pyridyl
S	n-butyl	OH	5-morpholino-3-pyridyl
S	n-butyl	OH	6-morpholino-3-pyridyl
S	n-butyl	OH	2-hydroxy-3-pyridyl
S	n-butyl	OH	4-hydroxy-3-pyridyl
S	n-butyl	OH	5-hydroxy-3-pyridyl
S	n-butyl	OH	6-hydroxy-3-pyridyl
S	n-butyl	OH	2-mercapto-3-pyridyl
S	n-butyl	OH	4-mercapto-3-pyridyl
S	n-butyl	OH	5-mercapto-3-pyridyl
S	n-butyl	OH	6-mercapto-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-butyl	OH	2-methylthio-3-pyridyl
S	n-butyl	OH	4-methylthio-3-pyridyl
S	n-butyl	OH	5-methylthio-3-pyridyl
S	n-butyl	OH	6-methylthio-3-pyridyl
S	n-butyl	OH	2,6-dimethyl-3-pyridyl
S	n-butyl	OH	5,6-dimethyl-3-pyridyl
S	n-butyl	OH	2,6-diethyl-3-pyridyl
S	n-butyl	OH	5,6-diethyl-3-pyridyl
S	n-butyl	OH	2,6-dimethoxy-3-pyridyl
S	n-butyl	OH	5,6-dimethoxy-3-pyridyl
S	n-butyl	OH	2,6-diethoxy-3-pyridyl
S	n-butyl	OH	5,6-diethoxy-3-pyridyl
S	n-butyl	OH	2,6-dichloro-3-pyridyl
S	n-butyl	OH	5,6-dichloro-3-pyridyl
S	n-butyl	OH	5-chloro-6-methoxy-3-pyridyl
S	n-butyl	OH	5-chloro-6-ethoxy-3-pyridyl
S	n-butyl	OH	2-chloro-6-methyl-3-pyridyl
S	n-butyl	OH	6-chloro-2-methyl-3-pyridyl
S	n-butyl	OH	2-methyl-4-pyridyl
S	n-butyl	OH	2-ethyl-4-pyridyl
S	n-butyl	OH	2-methoxy-4-pyridyl
S	n-butyl	OH	2-ethoxy-4-pyridyl
S	n-butyl	OH	2-chloro-4-pyridyl
S	n-butyl	OH	2-dimethylamino-4-pyridyl
S	n-butyl	OH	2-(1-pyrrolidinyl)-4-pyridyl
S	n-butyl	OH	2-piperidino-4-pyridyl
S	n-butyl	OH	2-morpholino-4-pyridyl
S	n-butyl	OH	2-methylthio-4-pyridyl
S	n-butyl	OH	2-pyrazinyl
S	n-butyl	OH	5-methyl-2-pyrazinyl
S	n-butyl	OH	5-ethyl-2-pyrazinyl
S	n-butyl	OH	5-methoxy-2-pyrazinyl
S	n-butyl	OH	5-ethoxy-2-pyrazinyl
S	n-butyl	OH	5-chloro-2-pyrazinyl
S	n-butyl	OH	6-methyl-2-pyrazinyl
S	n-butyl	OH	6-methoxy-2-pyrazinyl
S	n-butyl	OH	6-chloro-2-pyrazinyl
S	n-butyl	OCOOMe	2-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-butyl	OCOOMe	3-pyridyl
S	n-butyl	OCOOMe	4-pyridyl
S	n-butyl	OCOOMe	2-methyl-3-pyridyl
S	n-butyl	OCOOMe	4-methyl-3-pyridyl
S	n-butyl	OCOOMe	5-methyl-3-pyridyl
S	n-butyl	OCOOMe	6-methyl-3-pyridyl
S	n-butyl	OCOOMe	2-ethyl-3-pyridyl
S	n-butyl	OCOOMe	4-ethyl-3-pyridyl
S	n-butyl	OCOOMe	5-ethyl-3-pyridyl
S	n-butyl	OCOOMe	6-ethyl-3-pyridyl
S	n-butyl	OCOOMe	2-methoxy-3-pyridyl
S	n-butyl	OCOOMe	4-methoxy-3-pyridyl
S	n-butyl	OCOOMe	5-methoxy-3-pyridyl
S	n-butyl	OCOOMe	6-methoxy-3-pyridyl
S	n-butyl	OCOOMe	2-ethoxy-3-pyridyl
S	n-butyl	OCOOMe	4-ethoxy-3-pyridyl
S	n-butyl	OCOOMe	5-ethoxy-3-pyridyl
S	n-butyl	OCOOMe	6-ethoxy-3-pyridyl
S	n-butyl	OCOOMe	2-chloro-3-pyridyl
S	n-butyl	OCOOMe	4-chloro-3-pyridyl
S	n-butyl	OCOOMe	5-chloro-3-pyridyl
S	n-butyl	OCOOMe	6-chloro-3-pyridyl
S	n-butyl	OCOOMe	2-fluoro-3-pyridyl
S	n-butyl	OCOOMe	4-fluoro-3-pyridyl
S	n-butyl	OCOOMe	5-fluoro-3-pyridyl
S	n-butyl	OCOOMe	6-fluoro-3-pyridyl
S	n-butyl	OCOOMe	2-dimethylamino-3-pyridyl
S	n-butyl	OCOOMe	4-dimethylamino-3-pyridyl
S	n-butyl	OCOOMe	5-dimethylamino-3-pyridyl
S	n-butyl	OCOOMe	6-dimethylamino-3-pyridyl
S	n-butyl	OCOOMe	2-(1-pyrrolidinyl)-3-pyridyl
S	n-butyl	OCOOMe	3-(1-pyrrolidinyl)-3-pyridyl
S	n-butyl	OCOOMe	5-(1-pyrrolidinyl)-3-pyridyl
S	n-butyl	OCOOMe	6-(1-pyrrolidinyl)-3-pyridyl
S	n-butyl	OCOOMe	2-piperidino-3-pyridyl
S	n-butyl	OCOOMe	4-piperidino-3-pyridyl
S	n-butyl	OCOOMe	5-piperidino-3-pyridyl
S	n-butyl	OCOOMe	6-piperidino-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-butyl	OCOOMe	2-morpholino-3-pyridyl
S	n-butyl	OCOOMe	4-morpholino-3-pyridyl
S	n-butyl	OCOOMe	5-morpholino-3-pyridyl
S	n-butyl	OCOOMe	6-morpholino-3-pyridyl
S	n-butyl	OCOOMe	2-hydroxy-3-pyridyl
S	n-butyl	OCOOMe	4-hydroxy-3-pyridyl
S	n-butyl	OCOOMe	5-hydroxy-3-pyridyl
S	n-butyl	OCOOMe	6-hydroxy-3-pyridyl
S	n-butyl	OCOOMe	2-mercapto-3-pyridyl
S	n-butyl	OCOOMe	4-mercapto-3-pyridyl
S	n-butyl	OCOOMe	5-mercapto-3-pyridyl
S	n-butyl	OCOOMe	6-mercapto-3-pyridyl
S	n-butyl	OCOOMe	2-methylthio-3-pyridyl
S	n-butyl	OCOOMe	4-methylthio-3-pyridyl
S	n-butyl	OCOOMe	5-methylthio-3-pyridyl
S	n-butyl	OCOOMe	6-methylthio-3-pyridyl
S	n-butyl	OCOOMe	2,6-dimethyl-3-pyridyl
S	n-butyl	OCOOMe	5,6-dimethyl-3-pyridyl
S	n-butyl	OCOOMe	2,6-diethyl-3-pyridyl
S	n-butyl	OCOOMe	5,6-diethyl-3-pyridyl
S	n-butyl	OCOOMe	2,6-dimethoxy-3-pyridyl
S	n-butyl	OCOOMe	5,6-dimethoxy-3-pyridyl
S	n-butyl	OCOOMe	2,6-diethoxy-3-pyridyl
S	n-butyl	OCOOMe	5,6-diethoxy-3-pyridyl
S	n-butyl	OCOOMe	2,6-dichloro-3-pyridyl
S	n-butyl	OCOOMe	5,6-dichloro-3-pyridyl
S	n-butyl	OCOOMe	5-chloro-6-methoxy-3-pyridyl
S	n-butyl	OCOOMe	5-chloro-6-ethoxy-3-pyridyl
S	n-butyl	OCOOMe	2-chloro-6-methyl-3-pyridyl
S	n-butyl	OCOOMe	6-chloro-2-methyl-3-pyridyl
S	n-butyl	OCOOMe	2-methyl-4-pyridyl
S	n-butyl	OCOOMe	2-ethyl-4-pyridyl
S	n-butyl	OCOOMe	2-methoxy-4-pyridyl
S	n-butyl	OCOOMe	2-ethoxy-4-pyridyl
S	n-butyl	OCOOMe	2-chloro-4-pyridyl
S	n-butyl	OCOOMe	2-dimethylamino-4-pyridyl
S	n-butyl	OCOOMe	2-(1-pyrrolidinyl)-4-pyridyl
S	n-butyl	OCOOMe	2-piperidino-4-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-butyl	OCOOMe	2-morpholino-4-pyridyl
S	n-butyl	OCOOMe	2-methylthio-4-pyridyl
S	n-butyl	OCOOMe	2-pyrazinyl
S	n-butyl	OCOOMe	5-methyl-2-pyrazinyl
S	n-butyl	OCOOMe	5-ethyl-2-pyrazinyl
S	n-butyl	OCOOMe	5-methoxy-2-pyrazinyl
S	n-butyl	OCOOMe	5-ethoxy-2-pyrazinyl
S	n-butyl	OCOOMe	5-chloro-2-pyrazinyl
S	n-butyl	OCOOMe	6-methyl-2-pyrazinyl
S	n-butyl	OCOOMe	6-methoxy-2-pyrazinyl
S	n-butyl	OCOOMe	6-chloro-2-pyrazinyl
S	n-butyl	OCOOEt	2-pyridyl
S	n-butyl	OCOOEt	3-pyridyl
S	n-butyl	OCOOEt	4-pyridyl
S	n-butyl	OCOOEt	2-methyl-3-pyridyl
S	n-butyl	OCOOEt	4-methyl-3-pyridyl
S	n-butyl	OCOOEt	6-methyl-3-pyridyl
S	n-butyl	OCOOEt	6-methyl-3-pyridyl
S	n-butyl	OCOOEt	2-ethyl-3-pyridyl
S	n-butyl	OCOOEt	4-ethyl-3-pyridyl
S	n-butyl	OCOOEt	5-ethyl-3-pyridyl
S	n-butyl	OCOOEt	6-ethyl-3-pyridyl
S	n-butyl	OCOOEt	2-methoxy-3-pyridyl
S	n-butyl	OCOOEt	4-methoxy-3-pyridyl
S	n-butyl	OCOOEt	5-methoxy-3-pyridyl
S	n-butyl	OCOOEt	6-methoxy-3-pyridyl
S	n-butyl	OCOOEt	2-ethoxy-3-pyridyl
S	n-butyl	OCOOEt	4-ethoxy-3-pyridyl
S	n-butyl	OCOOEt	5-ethoxy-3-pyridyl
S	n-butyl	OCOOEt	6-ethoxy-3-pyridyl
S	n-butyl	OCOOEt	2-chloro-3-pyridyl
S	n-butyl	OCOOEt	4-chloro-3-pyridyl
S	n-butyl	OCOOEt	5-chloro-3-pyridyl
S	n-butyl	OCOOEt	6-chloro-3-pyridyl
S	n-butyl	OCOOEt	2-fluoro-3-pyridyl
S	n-butyl	OCOOEt	4-fluoro-3-pyridyl
S	n-butyl	OCOOEt	5-fluoro-3-pyridyl
S	n-butyl	OCOOEt	6-fluoro-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-butyl	OCOOEt	2-dimethylamino-3-pyridyl
S	n-butyl	OCOOEt	4-dimethylamino-3-pyridyl
S	n-butyl	OCOOET	5-dimethylamino-3-pyridyl
S	n-butyl	OCOOEt	6-dimethylamino-3-pyridyl
S	n-butyl	OCOOEt	2-(1-pyrrolidinyl)-3-pyridyl
S	n-butyl	OCOOEt	3-(1-pyrrolidinyl)-3-pyridyl
S	n-butyl	OCOOEt	5-(1-pyrrolidinyl)-3-pyridyl
S	n-butyl	OCOOEt	6-(1-pyrrolidinyl)-3-pyridyl
S	n-butyl	OCOOEt	2-piperidino-3-pyridyl
S	n-butyl	OCOOEt	4-piperidino-3-pyridyl
S	n-butyl	OCOOEt	5-piperidino-3-pyridyl
S	n-butyl	OCOOEt	6-piperidino-3-pyridyl
S	n-butyl	OCOOEt	2-morpholino-3-pyridyl
S	n-butyl	OCOOEt	4-morphalino-3-pyridyl
S	n-butyl	OCOOEt	5-morpholino-3-pyridyl
S	n-butyl	OCOOEt	6-morpholino-3-pyridyl
S	n-butyl	OCOOEt	2-hydroxy-3-pyridyl
S	n-butyl	OCOOEt	4-hydroxy-3-pyridyl
S	n-butyl	OCOOEt	5-hydroxy-3-pyridyl
S	n-butyl	OCOOEt	6-hydroxy-3-pyridyl
S	n-butyl	OCOOEt	2-mercapto-3-pyridyl
S	n-butyl	OCOOEt	4-mercapto-3-pyridyl
S	n-butyl	OCOOEt	5-mercapto-3-pyridyl
S	n-butyl	OCOOEt	6-mercapto-3-pyridyl
S	n-butyl	OCOOEt	2-methylthio-3-pyridyl
S	n-butyl	OCOOEt	4-methylthio-3-pyridyl
S	n-butyl	OCOOEt	5-methylthio-3-pyridyl
S	n-butyl	OCOOEt	6-methylthio-3-pyridyl
S	n-butyl	OCOOEt	2,6-dimethyl-3-pyridyl
S	n-butyl	OCOOEt	5,6-dimethyl-3-pyridyl
S	n-butyl	OCOOEt	2,6-diethyl-3-pyridyl
S	n-butyl	OCOOEt	5,6-diethyl-3-pyridyl
S	n-butyl	OCOOEt	2,6-dimethoxy-3-pyridyl
S	n-butyl	OCOOEt	5,6-dimethoxy-3-pyridyl
S	n-butyl	OCOOEt	2,6-diethoxy-3-pyridyl
S	n-butyl	OCOOEt	5,6-diethoxy-3-pyridyl
S	n-butyl	OCOOEt	2,6-dichloro-3-pyridyl
S	n-butyl	OCOOEt	5,6-dichloro-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-butyl	OCOOEt	5-chloro-6-methoxy-3-pyridyl
S	n-butyl	OCOOEt	5-chloro-6-ethoxy-3-pyridyl
S	n-butyl	OCOOEt	2-chloro-6-methyl-3-pyridyl
S	n-butyl	OCOOEt	6-chloro-2-methyl-3-pyridyl
S	n-butyl	OCOOEt	2-methyl-4-pyridyl
S	n-butyl	OCOOEt	2-ethyl-4-pyridyl
S	n-butyl	OCOOEt	2-methoxy-4-pyridyl
S	n-butyl	OCOOEt	2-ethoxy-4-pyridyl
S	n-butyl	OCOOEt	2-chloro-4-pyridyl
S	n-butyl	OCOOEt	2-dimethylamino-4-pyridyl
S	n-butyl	OCOOEt	2-(1-pyrrolidinyl)-4-pyridyl
S	n-butyl	OCOOEt	2-piperidino-4-pyridyl
S	n-butyl	OCOOEt	2-morpholino-4-pyridyl
S	n-butyl	OCOOEt	2-methylthio-4-pyridyl
S	n-butyl	OCOOEt	2-pyrazinyl
S	n-butyl	OCOOEt	5-methyl-2-pyrazinyl
S	n-butyl	OCOOEt	5-ethyl-2-pyrazinyl
S	n-butyl	OCOOEt	5-methoxy-2-pyrazinyl
S	n-butyl	OCOOEt	5-ethoxy-2-pyrazinyl
S	n-butyl	OCOOEt	5-chloro-2-pyrazinyl
S	n-butyl	OCOOEt	6-methyl-2-pyrazinyl
S	n-butyl	OCOOEt	6-methoxy-2-pyrazinyl
S	n-butyl	OCOOEt	6-chloro-2-pyrazinyl
S	n-pentyl	OH	2-pyridyl
S	n-pentyl	OH	3-pyridyl
S	n-pentyl	OH	4-pyridyl
S	n-pentyl	OH	2-methyl-3-pyridyl
S	n-pentyl	OH	4-methyl-3-pyridyl
S	n-pentyl	OH	5-methyl-3-pyridyl
S	n-pentyl	OH	6-methyl-3-pyridyl
S	n-pentyl	OH	2-ethyl-3-pyridyl
S	n-pentyl	OH	4-ethyl-3-pyridyl
S	n-pentyl	OH	5-ethyl-3-pyridyl
S	n-pentyl	OH	6-ethyl-3-pyridyl
S	n-pentyl	OH	2-methoxy-3-pyridyl
S	n-pentyl	OH	4-methoxy-3-pyridyl
S	n-pentyl	OH	5-methoxy-3-pyridyl
S	n-pentyl	OH	6-methoxy-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-pentyl	OH	2-ethoxy-3-pyridyl
S	n-pentyl	OH	4-ethoxy-3-pyridyl
S	n-pentyl	OH	5-ethoxy-3-pyridyl
S	n-pentyl	OH	6-ethoxy-3-pyridyl
S	n-pentyl	OH	2-chloro-3-pyridyl
S	n-pentyl	OH	4-chloro-3-pyridyl
S	n-pentyl	OH	5-chloro-3-pyridyl
S	n-pentyl	OH	6-chloro-3-pyridyl
S	n-pentyl	OH	2-fluoro-3-pyridyl
S	n-pentyl	OH	4-fluoro-3-pyridyl
S	n-pentyl	OH	5-fluoro-3-pyridyl
S	n-pentyl	OH	6-fluoro-3-pyridyl
S	n-pentyl	OH	2-dimethylamino-3-pyridyl
S	n-pentyl	OH	4-dimethylamino-3-pyridyl
S	n-pentyl	OH	5-dimethylamino-3-pyridyl
S	n-pentyl	OH	6-dimethylamino-3-pyridyl
S	n-pentyl	OH	2-(1-pyrrolidinyl)-3-pyridyl
S	n-pentyl	OH	3-(1-pyrrolidinyl)-3-pyridyl
S	n-pentyl	OH	5-(1-pyrrolidinyl)-3-pyridyl
S	n-pentyl	OH	6-(1-pyrrolidinyl)-3-pyridyl
S	n-pentyl	OH	2-piperidino-3-pyridyl
S	n-pentyl	OH	4-piperidino-3-pyridyl
S	n-pentyl	OH	5-piperidino-3-pyridyl
S	n-pentyl	OH	6-piperidino-3-pyridyl
S	n-pentyl	OH	2-morpholino-3-pyridyl
S	n-pentyl	OH	4-morpholino-3-pyridyl
S	n-pentyl	OH	5-morpholino-3-pyridyl
S	n-pentyl	OH	6-morpholino-3-pyridyl
S	n-pentyl	OH	2-hydroxy-3-pyridyl
S	n-pentyl	OH	4-hydroxy-3-pyridyl
S	n-pentyl	OH	5-hydroxy-3-pyridyl
S	n-pentyl	OH	6-hydroxy-3-pyridyl
S	n-pentyl	OH	2-mercapto-3-pyridyl
S	n-pentyl	OH	4-mercapto-3-pyridyl
S	n-pentyl	OH	5-mercapto-3-pyridyl
S	n-pentyl	OH	6-mercapto-3-pyridyl
S	n-pentyl	OH	2-methylthio-3-pyridyl
S	n-pentyl	OH	4-methylthio-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-pentyl	OH	5-methylthio-3-pyridyl
S	n-pentyl	OH	6-methylthio-3-pyridyl
S	n-pentyl	OH	2,6-dimethyl-3-pyridyl
S	n-pentyl	OH	5,6-dimethyl-3-pyridyl
S	n-pentyl	OH	2,6-diethyl-3-pyridyl
S	n-pentyl	OH	5,6-diethyl-3-pyridyl
S	n-pentyl	OH	2,6-dimethoxy-3-pyridyl
S	n-pentyl	OH	5,6-dimethoxy-3-pyridyl
S	n-pentyl	OH	2,6-diethoxy-3-pyridyl
S	n-pentyl	OH	5,6-diethoxy-3-pyridyl
S	n-pentyl	OH	2,6-dichloro-3-pyridyl
S	n-pentyl	OH	5,6-dichloro-3-pyridyl
S	n-pentyl	OH	5-chloro-6-methoxy-3-pyridyl
S	n-pentyl	OH	5-chloro-6-ethoxy-3-pyridyl
S	n-pentyl	OH	2-chloro-6-methyl-3-pyridyl
S	n-pentyl	OH	6-chloro-2-methyl-3-pyridyl
S	n-pentyl	OH	2-methyl-4-pyridyl
S	n-pentyl	OH	2-ethyl-4-pyridyl
S	n-pentyl	OH	2-methoxy-4-pyridyl
S	n-pentyl	OH	2-ethoxy-4-pyridyl
S	n-pentyl	OH	2-chloro-4-pyridyl
S	n-pentyl	OH	2-dimethylamino-4-pyridyl
S	n-pentyl	OH	2-(1-pyrrolidinyl)-4-pyridyl
S	n-pentyl	OH	2-piperidino-4-pyridyl
S	n-pentyl	OH	2-morpholino-4-pyridyl
S	n-pentyl	OH	2-methylthio-4-pyridyl
S	n-pentyl	OH	2-pyrazinyl
S	n-pentyl	OH	5-methyl-2-pyrazinyl
S	n-pentyl	OH	5-ethyl-2-pyrazinyl
S	n-pentyl	OH	5-methoxy-2-pyrazinyl
S	n-pentyl	OH	5-ethoxy-2-pyrazinyl
S	n-pentyl	OH	5-chloro-2-pyrazinyl
S	n-pentyl	OH	6-methyl-2-pyrazinyl
S	n-pentyl	OH	6-methoxy-2-pyrazinyl
S	n-pentyl	OH	6-chloro-2-pyrazinyl
S	n-pentyl	OCOOMe	2-pyridyl
S	n-pentyl	OCOOMe	3-pyridyl
S	n-pentyl	OCOOMe	4-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-pentyl	OCOOMe	2-methyl-3-pyridyl
S	n-pentyl	OCOOMe	4-methyl-3-pyridyl
S	n-pentyl	OCOOMe	5-methyl-3-pyridyl
S	n-pentyl	OCOOMe	6-methyl-3-pyridyl
S	n-pentyl	OCOOMe	2-ethyl-3-pyridyl
S	n-pentyl	OCOOMe	4-ethyl-3-pyridyl
S	n-pentyl	OCOOMe	5-ethyl-3-pyridyl
S	n-pentyl	OCOOMe	6-ethyl-3-pyridyl
S	n-pentyl	OCOOMe	2-methoxy-3-pyridyl
S	n-pentyl	OCOOMe	4-methoxy-3-pyridyl
S	n-pentyl	OCOOMe	5-methoxy-3-pyridyl
S	n-pentyl	OCOOMe	6-methoxy-3-pyridyl
S	n-pentyl	OCOOMe	2-ethoxy-3-pyridyl
S	n-pentyl	OCOOMe	4-ethoxy-3-pyridyl
S	n-pentyl	OCOOMe	5-ethoxy-3-pyridyl
S	n-pentyl	OCOOMe	6-ethoxy-3-pyridyl
S	n-pentyl	OCOOMe	2-chloro-3-pyridyl
S	n-pentyl	OCOOMe	4-chloro-3-pyridyl
S	n-pentyl	OCOOMe	5-chloro-3-pyridyl
S	n-pentyl	OCOOMe	6-chloro-3-pyridyl
S	n-pentyl	OCOOMe	2-fluoro-3-pyridyl
S	n-pentyl	OCOOMe	4-fluoro-3-pyridyl
S	n-pentyl	OCOOMe	5-fluoro-3-pyridyl
S	n-pentyl	OCOOMe	6-fluoro-3-pyridyl
S	n-pentyl	OCOOMe	2-dimethylamino-3-pyridyl
S	n-pentyl	OCOOMe	4-dimethylamino-3-pyridyl
S	n-pentyl	OCOOMe	5-dimethylamino-3-pyridyl
S	n-pentyl	OCOOMe	6-dimethylamino-3-pyridyl
S	n-pentyl	OCOOMe	2-(1-pyrrolidinyl)-3-pyridyl
S	n-pentyl	OCOOMe	3-(1-pyrrolidinyl)-3-pyridyl
S	n-pentyl	OCOOMe	5-(1-pyrrolidinyl)-3-pyridyl
S	n-pentyl	OCOOMe	6-(1-pyrrolidinyl)-3-pyridyl
S	n-pentyl	OCOOMe	2-piperidino-3-pyridyl
S	n-pentyl	OCOOMe	4-piperidino-3-pyridyl
S	n-pentyl	OCOOMe	5-piperidino-3-pyridyl
S	n-pentyl	OCOOMe	6-piperidino-3-pyridyl
S	n-pentyl	OCOOMe	2-morpholino-3-pyridyl
S	n-pentyl	OCOOMe	4-morpholino-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-pentyl	OCOOMe	5-morpholino-3-pyridyl
S	n-pentyl	OCOOMe	6-morpholino-3-pyridyl
S	n-pentyl	OCOOMe	2-hydroxy-3-pyridyl
S	n-pentyl	OCOOMe	4-hydzoxy-3-pyridyl
S	n-pentyl	OCOOMe	5-hydroxy-3-pyridyl
S	n-pentyl	OCOOMe	6-hydroxy-3-pyridyl
S	n-pentyl	OCOOMe	2-mercapto-3-pyridyl
S	n-pentyl	OCOOMe	4-mercapto-3-pyridyl
S	n-pentyl	OCOOMe	5-mercapto-3-pyridyl
S	n-pentyl	OCOOMe	6-mercapto-3-pyridyl
S	n-pentyl	OCOOMe	2-methylthio-3-pyridyl
S	n-pentyl	OCOOMe	4-methylthio-3-pyridyl
S	n-pentyl	OCOOMe	5-methylthio-3-pyridyl
S	n-pentyl	OCOOMe	6-methylthio-3-pyridyl
S	n-pentyl	OCOOMe	2,6-dimethyl-3-pyridyl
S	n-pentyl	OCOOMe	5,6-dimethyl-3-pyridyl
S	n-pentyl	OCOOMe	2,6-diethyl-3-pyridyl
S	n-pentyl	OCOOMe	5,6-diethyl-3-pyridyl
S	n-pentyl	OCOOMe	2,6-dimethoxy-3-pyridyl
S	n-pentyl	OCOOMe	5,6-dimethoxy-3-pyridyl
S	n-pentyl	OCOOMe	2,6-diethoxy-3-pyridyl
S	n-pentyl	OCOOMe	5,6-diethoxy-3-pyridyl
S	n-pentyl	OCOOMe	2,6-dichloro-3-pyridyl
S	n-pentyl	OCOOMe	5,6-dichloro-3-pyridyl
S	n-pentyl	OCOOMe	5-chloro-6-methoxy-3-pyridyl
S	n-pentyl	OCOOMe	5-chloro-6-ethoxy-3-pyridyl
S	n-pentyl	OCOOMe	2-chloro-6-methyl-3-pyridyl
S	n-pentyl	OCOOMe	6-chloro-2-methyl-3-pyridyl
S	n-pentyl	OCOOMe	2-methyl-4-pyridyl
S	n-pentyl	OCOOMe	2-ethyl-4-pyridyl
S	n-pentyl	OCOOMe	2-methoxy-4-pyridyl
S	n-pentyl	OCOOMe	2-ethoxy-4-pyridyl
S	n-pentyl	OCOOMe	2-chloro-4-pyridyl
S	n-pentyl	OCOOMe	2-dimethylamino-4-pyridyl
S	n-pentyl	OCOOMe	2-(1-pyrrolidinyl)-4-pyridyl
S	n-pentyl	OCOOMe	2-piperidino-4-pyridyl
S	n-pentyl	OCOOMe	2-morpholino-4-pyridyl
S	n-pentyl	OCOOMe	2-methylthio-4-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-pentyl	OCOOMe	2-pyrazinyl
S	n-pentyl	OCOOMe	5-methyl-2-pyrazinyl
S	n-pentyl	OCOOMe	5-ethyl-2-pyrazinyl
S	n-pentyl	OCOOMe	5-methoxy-2-pyrazinyl
S	n-pentyl	OCOOMe	5-ethoxy-2-pyrazinyl
S	n-pentyl	OCOOMe	5-chloro-2-pyrazinyl
S	n-pentyl	OCOOMe	6-methyl-2-pyrazinyl
S	n-pentyl	OCOOMe	6-methoxy-2-pyrazinyl
S	n-pentyl	OCOOMe	6-chloro-2-pyrazinyl
S	n-pentyl	OCOOEt	2-pyridyl
S	n-pentyl	OCOOEt	3-pyridyl
S	n-pentyl	OCOOEt	4-pyridyl
S	n-pentyl	OCOOEt	2-methyl-3-pyridyl
S	n-pentyl	OCOOEt	4-methyl-3-pyridyl
S	n-pentyl	OCOOEt	5-methyl-3-pyridyl
S	n-pentyl	OCOOEt	6-methyl-3-pyridyl
S	n-pentyl	OCOOEt	2-ethyl-3-pyridyl
S	n-pentyl	OCOOEt	4-ethyl-3-pyridyl
S	n-pentyl	OCOOEt	5-ethyl-3-pyridyl
S	n-pentyl	OCOOEt	6-ethyl-3-pyridyl
S	n-pentyl	OCOOEt	2-methoxy-3-pyridyl
S	n-pentyl	OCOOEt	4-methoxy-3-pyridyl
S	n-pentyl	OCOOEt	5-methoxy-3-pyridyl
S	n-pentyl	OCOOEt	6-methoxy-3-pyridyl
S	n-pentyl	OCOOEt	2-ethoxy-3-pyridyl
S	n-pentyl	OCOOEt	4-ethoxy-3-pyridyl
S	n-pentyl	OCOOEt	5-ethoxy-3-pyridyl
S	n-pentyl	OCOOEt	6-ethoxy-3-pyridyl
S	n-pentyl	OCOOEt	2-chloro-3-pyridyl
S	n-pentyl	OCOOEt	4-chloro-3-pyridyl
S	n-pentyl	OCOOEt	5-chloro-3-pyridyl
S	n-pentyl	OCOOEt	6-chloro-3-pyridyl
S	n-pentyl	OCOOEt	2-fluoro-3-pyridyl
S	n-pentyl	OCOOEt	4-fluoro-3-pyridyl
S	n-pentyl	OCOOEt	5-fluoro-3-pyridyl
S	n-pentyl	OCOOEt	6-fluoro-3-pyridyl
S	n-pentyl	OCOOEt	2-dimethylamino-3-pyridyl
S	n-pentyl	OCOOEt	4-dimethylamino-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-pentyl	OCOOEt	5-dimethylamino-3-pyridyl
S	n-pentyl	OCOOEt	6-dimethylamino-3-pyridyl
S	n-pentyl	OCOOEt	2-(1-pyrrolidinyl)-3-pyridyl
S	n-pentyl	OCOOEt	3-(1-pyrrolidinyl)-3-pyridyl
S	n-pentyl	OCOOEt	5-(1-pyrrolidinyl)-3-pyridyl
S	n-pentyl	OCOOEt	6-(1-pyrrolidinyl)-3-pyridyl
S	n-pentyl	OCOOEt	2-piperidino-3-pyridyl
S	n-pentyl	OCOOEt	4-piperidino-3-pyridyl
S	n-pentyl	OCOOEt	5-piperidino-3-pyridyl
S	n-pentyl	OCOOEt	6-piperidino-3-pyridyl
S	n-pentyl	OCOOEt	2-morpholino-3-pyridyl
S	n-pentyl	OCOOEt	4-morpholino-3-pyridyl
S	n-pentyl	OCOOEt	5-morpholino-3-pyridyl
S	n-pentyl	OCOOEt	6-morpholino-3-pyridyl
S	n-pentyl	OCOOEt	2-hydroxy-3-pyridyl
S	n-pentyl	OCOOEt	4-hydroxy-3-pyridyl
S	n-pentyl	OCOOEt	5-hydroxy-3-pyridyl
S	n-pentyl	OCOOEt	6-hydroxy-3-pyridyl
S	n-pentyl	OCOOEt	2-mercapto-3-pyridyl
S	n-pentyl	OCOOEt	4-mercapto-3-pyridyl
S	n-pentyl	OCOOEt	.5-mercapto-3-pyridyl
S	n-pentyl	OCOOEt	6-mercapto-3-pyridyl
S	n-pentyl	OCOOEt	2-methylthio-3-pyridyl
S	n-pentyl	OCOOEt	4-methylthio-3-pyridyl
S	n-pentyl	OCOOEt	5-methylthio-3-pyridyl
S	n-pentyl	OCOOEt	6-methylthio-3-pyridyl
S	n-pentyl	OCOOEt	2,6-dimethyl-3-pyridyl
S	n-pentyl	OCOOEt	5,6-dimethyl-3-pyridyl
S	n-pentyl	OCOOEt	2,6-diethyl-3-pyridyl
S	n-pentyl	OCOOEt	5,6-diethyl-3-pyridyl
S	n-pentyl	OCOOEt	2,6-dimethoxy-3-pyridyl
S	n-pentyl	OCOOEt	5,6-dimethoxy-3-pyridyl
S	n-pentyl	OCOOEt	2,6-diethoxy-3-pyridyl
S	n-pentyl	OCOOEt	5,6-diethoxy-3-pyridyl
S	n-pentyl	OCOOEt	2,6-dichloro-3-pyridyl
S	n-pentyl	OCOOEt	5,6-dichloro-3-pyridyl
S	n-pentyl	OCOOEt	5-chloro-6-methoxy-3-pyridyl
S	n-pentyl	OCOOEt	5-chloro-6-ethoxy-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-pentyl	OCOOEt	2-chloro-8-methyl-3-pyridyl
S	n-pentyl	OCOOEt	6-chloro-2-methyl-3-pyridyl
S	n-pentyl	OCOOEt	2-methyl-4-pyridyl
S	n-pentyl	OCOOEt	2-ethyl-4-pyridyl
S	n-pentyl	OCOOEt	2-methoxy-4-pyridyl
S	n-pentyl	OCOOEt	2-ethoxy-4-pyridyl
S	n-pentyl	OCOOEt	2-chloro-4-pyridyl
S	n-pentyl	OCOOEt	2-dimethylamino-4-pyridyl
S	n-pentyl	OCOOEt	2-(1-pyrrolidinyl)-4-pyridyl
S	n-pentyl	OCOOEt	2-piperidino-4-pyridyl
S	n-pentyl	OCOOEt	2-morpholino-4-pyridyl
S	n-pentyl	OCOOEt	2-methylthio-4-pyridyl
S	n-pentyl	OCOOEt	2-pyrazinyl
S	n-pentyl	OCOOEt	5-methyl-2-pyrazinyl
S	n-pentyl	OCOOEt	5-ethyl-2-pyrazinyl
S	n-pentyl	OCOOEt	5-methoxy-2-pyrazinyl
S	n-pentyl	OCOOEt	5-ethoxy-2-pyrazinyl
S	n-pentyl	OCOOEt	5-chloro-2-pyrazinyl
S	n-pentyl	OCOOEt	6-methyl-2-pyrazinyl
S	n-pentyl	OCOOEt	6-methoxy-2-pyrazinyl
S	n-pentyl	OCOOEt	6-chloro-2-pyrazinyl
NH	2-methoxyethyl	OH	3-pyridyl
NH	2-methoxyethyl	OH	4-pyridyl
NH	2-methoxyethyl	OH	2-methyl-3-pyridyl
NH	2-methoxyethyl	OH	6-methyl-3-pyridyl
NH	2-methoxyethyl	OH	2-ethyl-3-pyridyl
NH	2-methoxyethyl	OH	6-ethyl-3-pyridyl
NH	2-methoxyethyl	OH	6-methoxy-3-pyridyl
NH	2-methoxyethyl	OH	6-ethoxy-3-pyridyl
NH	2-methoxyethyl	OH	2-chloro-3-pyridyl
NH	2-methoxyethyl	OH	6-chloro-3-pyridyl
NH	2-methoxyethyl	OH	5,6-dimethyl-3-pyridyl
NH	2-methoxyethyl	OH	5,6-dimethoxy-3-pyridyl
NH	2-methoxyethyl	OH	5,6-dichloro-3-pyridyl
NH	2-methoxyethyl	OH	6-dimethylamino-3-pyridyl
NH	2-methoxyethyl	OH	6-(1-pyrrolidinyl)-3-pyridyl
NH	2-methoxyethyl	OH	6-piperidino-3-pyridyl
NH	2-methoxyethyl	OH	6-morpholino-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
NH	2-methoxyethyl	OH	6-methylthio-3-pyridyl
NH	2-methoxyethyl	OH	2-pyrazinyl
NH	2-methoxyethyl	OH	5-methyl-2-pyrazinyl
NH	3-methoxypropyl	OH	3-pyridyl
NH	3-methoxypropyl	OH	4-pyridyl
NH	3-methoxypropyl	OH	2-methyl-3-pyridyl
NH	3-methoxypropyl	OH	6-methyl-3-pyridyl
NH	3-methoxypropyl	OH	2-ethyl-3-pyridyl
NH	3-methoxypropyl	OH	6-ethyl-3-pyridyl
NH	3-methoxypropyl	OH	2-methoxy-3-pyridyl
NH	3-methoxypropyl	OH	6-methoxy-3-pyridyl
NH	3-methoxypropyl	OH	6-ethoxy-3-pyridyl
NH	3-methoxypropyl	OH	2-chloro-3-pyridyl
NH	3-methoxypropyl	OH	6-chloro-3-pyridyl
NH	3-methoxypropyl	OH	5,6-dimethyl-3-pyridyl
NH	3-methoxypropyl	OH	5,6-dimethoxy-3-pyridyl
NH	3-methoxypropyl	OH	5,6-dichloro-3-pyridyl
NH	3-methoxypropyl	OH	6-dimethylamino-3-pyridyl
NH	3-methoxypropyl	OH	6-(1-pyrrolidinyl)-3-pyridyl
NH	3-methoxypropyl	OH	6-piperidino-3-pyridyl
NH	3-methoxypropyl	OH	6-morpholino-3-pyridyl
NH	3-methoxypropyl	OH	6-methylthio-3-pyridyl
NH	3-methoxypropyl	OH	2-pyrazinyl
NH	3-methoxypropyl	OH	5-methyl-2-pyrazinyl
O	2-methoxyethyl	OH	3-pyridyl
O	2-methoxyethyl	OH	4-pyridyl
O	2-methoxyethyl	OH	2-methyl-3-pyridyl
O	2-methoxyethyl	OH	6-methyl-3-pyridyl
O	2-methoxyethyl	OH	2-ethyl-3-pyridyl
O	2-methoxyethyl	OH	6-ethyl-3-pyridyl
O	2-methoxyethyl	OH	6-methoxy-3-pyridyl
O	2-methoxyethyl	OH	6-ethoxy-3-pyridyl
O	2-methoxyethyl	OH	2-chloro-3-pyridyl
O	2-methoxyethyl	OH	6-chloro-3-pyridyl
O	2-methoxyethyl	OH	5,6-dimethyl-3-pyridyl
O	2-methoxyethyl	OH	5,6-dimethoxy-3-pyridyl
O	2-methoxyethyl	OH	5,6-dichloro-3-pyridyl
O	2-methoxyethyl	OH	6-dimethylamino-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
O	2-methoxyethyl	OH	6-(1-pyrrolidinyl)-3-pyridyl
O	2-methoxyethyl	OH	6-piperidino-3-pyridyl
O	2-methoxyethyl	OH	6-morpholino-3-pyridyl
O	2-methoxyethyl	OH	6-methylthio-3-pyridyl
O	2-methoxyethyl	OH	2-pyrazinyl
O	2-methoxyethyl	OH	5-methyl-2-pyrazinyl
O	3-methoxypropyl	OH	3-pyridyl
O	3-methoxypropyl	OH	4-pyridyl
O	3-methoxypropyl	OH	2-methyl-3-pyridyl
O	3-methoxypropyl	OH	6-methyl-3-pyridyl
O	3-methoxypropyl	OH	2-ethyl-3-pyridyl
O	3-methoxypropyl	OH	6-ethyl-3-pyridyl
O	3-methoxypropyl	OH	2-methoxy-3-pyridyl
O	3-methoxypropyl	OH	6-methoxy-3-pyridyl
O	3-methoxypropyl	OH	6-ethoxy-3-pyridyl
O	3-methoxypropyl	OH	2-chloro-3-pyridyl
O	3-methoxypropyl	OH	6-chloro-3-pyridyl
O	3-methoxypropyl	OH	5,6-dimethyl-3-pyridyl
O	3-methoxypropyl	OH	5,6-dimethoxy-3-pyridyl
O	3-methoxypropyl	OH	5,6-dichloro-3-pyridyl
O	3-methoxypropyl	OH	6-dimethylamino-3-pyridyl
O	3-methoxypropyl	OH	6-(1-pyrrolidinyl)-3-pyridyl
O	3-methoxypropyl	OH	6-piperidino-3-pyridyl
O	3-methoxypropyl	OH	6-morpholino-3-pyridyl
O	3-methoxypropyl	OH	6-methylthio-3-pyridyl
O	3-methoxypropyl	OH	2-pyrazinyl
O	3-methoxypropyl	OH	5-methyl-2-pyrazinyl
S	2-methoxyethyl	OH	3-pyridyl
S	2-methoxyethyl	OH	4-pyridyl
S	2-methoxyethyl	OH	2-methyl-3-pyridyl
S	2-methoxyethyl	OH	6-methyl-3-pyridyl
S	2-methoxyethyl	OH	2-ethyl-3-pyridyl
S	2-methoxyethyl	OH	6-ethyl-3-pyridyl
S	2-methoxyethyl	OH	6-methoxy-3-pyridyl
S	2-methoxyethyl	OH	6-ethoxy-3-pyridyl
S	2-methoxyethyl	OH	2-chloro-3-pyridyl
S	2-methoxyethyl	OH	6-chloro-3-pyridyl
S	2-methoxyethyl	OH	5,6-dimethyl-3-pyridyl

Table 1 (continued)

X	R^1	R^2	Y
S	2-methoxyethyl	OH	5,6-dimethoxy-3-pyridyl
S	2-methoxyethyl	OH	5,6-dichloro-3-pyridyl
S	2-methoxyethyl	OH	6-dimethylamino-3-pyridyl
S	2-methoxyethyl	OH	6-(1-pyrrolidinyl)-3-pyridyl
S	2-methoxyethyl	OH	6-piperidino-3-pyridyl
S	2-methoxyethyl	OH	6-morpholino-3-pyridyl
S	2-methoxyethyl	OH	6-methylthio-3-pyridyl
S	2-methoxyethyl	OH	2-pyrazinyl
S	2-methoxyethyl	OH	5-methyl-2-pyrazinyl
S	2-hydroxyethyl	OH	3-pyridyl
S	2-hydroxyethyl	OH	4-pyridyl
S	2-hydroxyethyl	OH	2-methyl-3-pyridyl
S	2-hydroxyethyl	OH	6-methyl-3-pyridyl
S	2-hydroxyethyl	OH	2-ethyl-3-pyridyl
S	2-hydroxyethyl	OH	6-ethyl-3-pyridyl
S	2-hydroxyethyl	OH	2-methoxy-3-pyridyl
S	2-hydroxyethyl	OH	6-methoxy-3-pyridyl
S	2-hydroxyethyl	OH	6-ethoxy-3-pyridyl
S	2-hydroxyethyl	OH	2-chloro-3-pyridyl
S	2-hydroxyethyl	OH	6-chloro-8-pyridyl
S	2-hydroxyethyl	OH	5,6-dimethyl-3-pyridyl
S	2-hydroxyethyl	OH	5,6-dimethoxy-3-pyridyl
S	2-hydroxyethyl	OH	5,6-dichloro-3-pyridyl
S	2-hydroxyethyl	OH	6-dimethylamino-3-pyridyl
S	2-hydroxyethyl	OH	6-(1-pyrrolidinyl)-3-pyridyl
S	2-hydroxyethyl	OH	6-piperidino-3-pyridyl
S	2-hydroxyethyl	OH	6-morpholino-3-pyridyl
S	2-hydroxyethyl	OH	6-methylthio-3-pyridyl
S	2-hydroxyethyl	OH	2-pyrazinyl
S	2-hydroxyethyl	OH	5-methyl-2-pyrazinyl
NH	propyl	OH	1-naphthyl
NH	propyl	OH	2-naphthyl
NH	propyl	OH	2-pyrrolyl
NH	propyl	OH	3-pyrrolyl
NH	propyl	OH	2-furyl
NH	propyl	OH	3-furyl
NH	propyl	OH	2-thienyl
NH	propyl	OH	3-thienyl

Table 1 (continued)

X	R^1	R^2	Y
NH	propyl	OH	3-pyrazolyl
NH	propyl	OH	4-pyrazolyl
NH	propyl	OH	2-imidazolyl
NH	propyl	OH	4-imidazolyl
NH	propyl	OH	2-oxazolyl
NH	propyl	OH	4-oxazolyl
NH	propyl	OH	5-oxazolyl
NH	propyl	OH	2-thiazolyl
NH	propyl	OH	4-thiazolyl
NH	propyl	OH	5-thiazolyl
NH	propyl	OH	2-pyrimidinyl
NH	propyl	OH	4-pyrimidinyl
NH	propyl	OH	5-pyrimidinyl
NH	propyl	OH	2-indolyl
NH	propyl	OH	3-indolyl
NH	propyl	OH	5-indolyl
NH	propyl	OH	6-indolyl
NH	propyl	OH	5-benzimidazolyl
NH	propyl	OH	2-benzofuryl
NH	propyl	OH	3-indazolyl
NH	propyl	OH	2-benzoxazolyl
NH	propyl	OH	4-fluoro-1-naphthyl
NH	propyl	OH	5-chloro-2-thienyl
NH	propyl	OH	4-methyl-1-naphthyl
NH	propyl	OH	1-methyl-2-pyrrolyl
NH	propyl	OH	2-methyl-3-furyl
NH	propyl	OH	5-methyl-2-thienyl
NH	propyl	OH	4-methyl-5-imidazolyl
NH	propyl	OH	1-methyl-3-indolyl
NH	propyl	OH	2-methoxy-1-naphthyl
NH	propyl	OH	3-methoxy-2-naphthyl
NH	propyl	OH	6-ethoxy-2-naphthyl
NH	propyl	OH	5-methoxy-3-indolyl
NH	propyl	OH	1,4-dimethoxy-2-naphthyl
NH	propyl	OH	5,6-dimethoxy-2-indolyl
NH	propyl	OH	5-methoxy-1-methyl-2-indolyl
NH	propyl	OCOOMe	1-naphthyl
NH	propyl	OCOOMe	2-naphthyl

Table 1 (continued)

X	R^1	R^2	Y
NH	propyl	OCOOMe	2-pyrrolyl
NH	propyl	OCOOMe	3-pyrrolyl
NH	propyl	OCOOMe	2-furyl
NH	propyl	OCOOMe	3-furyl
NH	propyl	OCOOMe	2-thienyl
NH	propyl	OCOOMe	3-thienyl
NH	propyl	OCOOMe	3-pyrazolyl
NH	propyl	OCOOMe	4-pyrazolyl
NH	propyl	OCOOMe	2-imidazolyl
NH	propyl	OCOOMe	4-imidazolyl
NH	propyl	OCOOMe	2-oxazolyl
NH	propyl	OCOOMe	4-oxazolyl
NH	propyl	OCOOMe	5-oxazolyl
NH	propyl	OCOOMe	2-thiazolyl
NH	propyl	OCOOMe	4-thiazolyl
NH	propyl	OCOOMe	5-thiazolyl
NH	propyl	OCOOMe	2-pyrimidinyl
NH	propyl	OCOOMe	4-pyrimidinyl
NH	propyl	OCOOMe	5-pyrimidinyl
NH	propyl	OCOOMe	2-indolyl
NH	propyl	OCOOMe	3-indolyl
NH	propyl	OCOOMe	5-indolyl
NH	propyl	OCOOMe	6-indolyl
NH	propyl	OCOOMe	5-benzimidazolyl
NH	propyl	OCOOMe	2-benzofuryl
NH	propyl	OCOOMe	3-indazolyl
NH	propyl	OCOOMe	2-benzoxazolyl
NH	propyl	OCOOMe	4-fluoro-1-naphthyl
NH	propyl	OCOOMe	5-chloro-2-thienyl
NH	propyl	OCOOMe	4-methyl-1-naphthyl
NH	propyl	OCOOMe	1-methyl-2-pyrrolyl
NH	propyl	OCOOMe	2-methyl-3-furyl
NH	propyl	OCOOMe	5-methyl-2-thienyl
NH	propyl	OCOOMe	4-methyl-5-imidazolyl
NH	propyl	OCOOMe	1-methyl-3-indolyl
NH	propyl	OCOOMe	2-methoxy-1-naphthyl
NH	propyl	OCOOMe	3-methoxy-2-naphthyl
NH	propyl	OCOOMe	6-ethoxy-2-naphthyl

Table 1 (continued)

X	R^1	R^2	Y
NH	propyl	OCOOMe	5-methoxy-3-indolyl
NH	propyl	OCOOMe	1,4-dimethoxy-2-naphthyl
NH	propyl	OCOOMe	5,6-dimethoxy-2-indolyl
NH	propyl	OCOOMe	5-methoxy-1-methyl-2-indolyl
NH	propyl	OCOOEt	1-naphthyl
NH	propyl	OCOOEt	2-naphthyl
NH	propyl	OCOOEt	2-pyrrolyl
NH	propyl	OCOOEt	3-pyrrolyl
NH	propyl	OCOOEt	2-furyl
NH	propyl	OCOOEt	3-furyl
NH	propyl	OCOOEt	2-thienyl
NH	propyl	OCOOEt	3-thienyl
NH	propyl	OCOOEt	3-pyrazolyl
NH	propyl	OCOOEt	4-pyrazolyl
NH	propyl	OCOOEt	2-imidazolyl
NH	propyl	OCOOEt	4-imidazolyl
NH	propyl	OCOOEt	2-oxazolyl
NH	propyl	OCOOEt	4-oxazolyl
NH	propyl	OCOOEt	5-oxazolyl
NH	propyl	OCOOEt	2-thiazolyl
NH	propyl	OCOOEt	4-thiazolyl
NH	propyl	OCOOEt	5-thiazolyl
NH	propyl	OCOOEt	2-pyrimidinyl
NH	propyl	OCOOEt	4-pyrimidinyl
NH	propyl	OCOOEt	5-pyrimidinyl
NH	propyl	OCOOEt	2-indolyl
NH	propyl	OCOOEt	3-indolyl
NH	propyl	OCOOEt	5-indolyl
NH	propyl	OCOOEt	6-indolyl
NH	propyl	OCOOEt	5-benzimidazolyl
NH	propyl	OCOOEt	2-benzofuryl
NH	propyl	OCOOEt	3-indazolyl
NH	propyl	OCOOEt	2-benzoxazolyl
NH	propyl	OCOOEt	4-fluoro-1-naphthyl
NH	propyl	OCOOEt	5-chloro-2-thienyl
NH	propyl	OCOOEt	4-methyl-1-naphthyl
NH	propyl	OCOOEt	1-methyl-2-pyrrolyl
NH	propyl	OCOOEt	2-methyl-3-furyl

Table 1 (continued)

X	R^1	R^2	Y
NH	propyl	OCOOEt	5-methyl-2-thienyl
NH	propyl	OCOOEt	4-methyl-5-imidazolyl
NH	propyl	OCOOEt	1-methyl-3-indolyl
NH	propyl	OCOOEt	2-methoxy-1-naphthyl
NH	propyl	OCOOEt	3-methoxy-2-naphthyl
NH	propyl	OCOOEt	6-ethoxy-2-naphthyl
NH	propyl	OCOOEt	5-methoxy-3-indolyl
NH	propyl	OCOOEt	1,4-dimethoxy-2-naphthyl
NH	propyl	OCOOEt	5,6-dimetboxy-2-indolyl
NH	propyl	OCOOEt	5-methoxy-1-methyl-2-indolyl
NH	n-butyl	OH	1-naphthyl
NH	n-butyl	OH	2-naphthyl
NH	n-butyl	OH	2-pyrrolyl
NH	n-butyl	OH	3-pyrrolyl
NH	n-butyl	OH	2-furyl
NH	n-butyl	OH	3-furyl
NH	n-butyl	OH	2-thienyl
NH	n-butyl	OH	3-thienyl
NH	n-butyl	OH	3-pyrazolyl
NH	n-butyl	OH	4-pyrazolyl
NH	n-butyl	OH	2-imidazolyl
NH	n-butyl	OH	4-imidazolyl
NH	n-butyl	OH	2-oxazolyl
NH	n-butyl	OH	4-oxazolyl
NH	n-butyl	OH	5-oxazolyl
NH	n-butyl	OH	2-thiazolyl
NH	n-butyl	OH	4-thiazolyl
NH	n-butyl	OH	5-thiazolyl
NH	n-butyl	OH	2-pyrimidinyl
NH	n-butyl	OH	4-pyrimidinyl
NH	n-butyl	OH	5-pyrimidinyl
NH	n-butyl	OH	2-indolyl
NH	n-butyl	OH	3-indolyl
NH	n-butyl	OH	5-indolyl
NH	n-butyl	OH	6-indolyl
NH	n-butyl	OH	5-benzimidazolyl
NH	n-butyl	OH	2-benzofuryl
NH	n-butyl	OH	3-indazolyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-butyl	OH	2-benzoxazolyl
NH	n-butyl	OH	4-fluoro-1-naphthyl
NH	n-butyl	OH	5-chloro-2-thienyl
NH	n-butyl	OH	4-methyl-1-naphthyl
NH	n-butyl	OH	1-methyl-2-pyrrolyl
NH	n-butyl	OH	2-methyl-3-furyl
NH	n-butyl	OH	5-methyl-2-thienyl
NH	n-butyl	OH	4-methyl-5-imidazolyl
NH	n-butyl	OH	1-methyl-3-indolyl
NH	n-butyl	OH	2-methoxy-1-naphthyl
NH	n-butyl	OH	3-methoxy-2-naphthyl
NH	n-butyl	OH	6-ethoxy-2-naphthyl
NH	n-butyl	OH	5-methoxy-3-indolyl
NH	n-butyl	OH	1,4-dimethoxy-2-naphthyl
NH	n-butyl	OH	5,6-dimethoxy-2-indolyl
NH	n-butyl	OH	5-methoxy-1-methyl-2-indolyl
NH	n-butyl	OCOOMe	1-naphthyl
NH	n-butyl	OCOOMe	2-naphthyl
NH	n-butyl	OCOOMe	2-pyrrolyl
NH	n-butyl	OCOOMe	3-pyrrolyl
NH	n-butyl	OCOOMe	2-furyl
NH	n-butyl	OCOOMe	3-furyl
NH	n-butyl	OCOOMe	2-thienyl
NH	n-butyl	OCOOMe	3-thienyl
NH	n-butyl	OCOOMe	3-pyrazolyl
NH	n-butyl	OCOOMe	4-pyrazolyl
NH	n-butyl	OCOOMe	2-imidazolyl
NH	n-butyl	OCOOMe	4-imidazolyl
NH	n-butyl	OCOOMe	2-oxazolyl
NH	n-butyl	OCOOMe	4-oxazolyl
NH	n-butyl	OCOOMe	5-oxazolyl
NH	n-butyl	OCOOMe	2-thiazolyl
NH	n-butyl	OCOOMe	4-thiazolyl
NH	n-butyl	OCOOMe	5-thiazolyl
NH	n-butyl	OCOOMe	2-pyrimidinyl
NH	n-butyl	OCOOMe	4-pyrimidinyl
NH	n-butyl	OCOOMe	5-pyrimidinyl
NH	n-butyl	OCOOMe	2-indolyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-butyl	OCOOMe	3-indolyl
NH	n-butyl	OCOOMe	5-indolyl
NH	n-butyl	OCOOMe	6-indolyl
NH	n-butyl	OCOOMe	5-benzimidazolyl
NH	n-butyl	OCOOMe	2-benzofuryl
NH	n-butyl	OCOOMe	3-indazolyl
NH	n-butyl	OCOOMe	2-benzoxazolyl
NH	n-butyl	OCOOMe	4-fluoro-1-naphthyl
NH	n-butyl	OCOOMe	5-chloro-2-thienyl
NH	n-butyl	OCOOMe	4-methyl-1-naphthyl
NH	n-butyl	OCOOMe	1-methyl-2-pyrrolyl
NH	n-butyl	OCOOMe	2-methyl-3-furyl
NH	n-butyl	OCOOMe	5-methyl-2-thienyl
NH	n-butyl	OCOOMe	4-methyl-5-imidazolyl
NH	n-butyl	OCOOMe	1-methyl-3-indolyl
NH	n-butyl	OCOOMe	2-methoxy-1-naphthyl
NH	n-butyl	OCOOMe	3-methoxy-2-naphthyl
NH	n-butyl	OCOOMe	6-ethoxy-2-naphthyl
NH	n-butyl	OCOOMe	5-methoxy-3-indolyl
NH	n-butyl	OCOOMe	1,4-dimethoxy-2-naphthyl
NH	n-butyl	OCOOMe	5,6-dimethoxy-2-indolyl
NH	n-butyl	OCOOMe	5-methoxy-1-methyl-2-indolyl
NH	n-butyl	OCOOEt	1-naphthyl
NH	n-butyl	OCOOEt	2-naphthyl
NH	n-butyl	OCOOEt	2-pyrrolyl
NH	n-butyl	OCOOEt	3-pyrrolyl
NH	n-butyl	OCOOEt	2-furyl
NH	n-butyl	OCOOEt	3-furyl
NH	n-butyl	OCOOEt	2-thienyl
NH	n-butyl	OCOOEt	3-thienyl
NH	n-butyl	OCOOEt	3-pyrazolyl
NH	n-butyl	OCOOEt	4-pyrazolyl
NH	n-butyl	OCOOEt	2-imidazolyl
NH	n-butyl	OCOOEt	4-imidazolyl
NH	n-butyl	OCOOEt	2-oxazolyl
NH	n-butyl	OCOOEt	4-oxazolyl
NH	n-butyl	OCOOEt	5-oxazolyl
NH	n-butyl	OCOOEt	2-thiazolyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-butyl	OCOOEt	4-thiazolyl
NH	n-butyl	OCOOEt	5-thiazolyl
NH	n-butyl	OCOOEt	2-pyrimidinyl
NH	n-butyl	OCOOEt	4-pyrimidinyl
NH	n-butyl	OCOOEt	5-pyrimidinyl
NH	n-butyl	OCOOEt	2-indolyl
NH	n-butyl	OCOOEt	3-indolyl
NH	n-butyl	OCOOEt	5-indolyl
NH	n-butyl	OCOOEt	6-indolyl
NH	n-butyl	OCOOEt	5-benzimidazolyl
NH	n-butyl	OCOOEt	2-benzofuryl
NH	n-butyl	OCOOEt	3-indazolyl
NH	n-butyl	OCOOEt	2-benzoxazolyl
NH	n-butyl	OCOOEt	4-fluoro-1-naphthyl
NH	n-butyl	OCOOEt	5-chloro-2-thienyl
NH	n-butyl	OCOOEt	4-methyl-1-naphthyl
NH	n-butyl	OCOOEt	1-methyl-2-pyrrolyl
NH	n-butyl	OCOOEt	2-methyl-3-furyl
NH	n-butyl	OCOOEt	5-methyl-2-thienyl
NH	n-butyl	OCOOEt	4-methyl-5-imidazolyl
NH	n-butyl	OCOOEt	1-methyl-3-indolyl
NH	n-butyl	OCOOEt	2-methoxy-1-naphthyl
NH	n-butyl	OCOOEt	3-methoxy-2-naphthyl
NH	n-butyl	OCOOEt	6-ethoxy-2-naphthyl
NH	n-butyl	OCOOEt	5-methoxy-3-indolyl
NH	n-butyl	OCOOEt	1,4-dimethoxy-2-naphthyl
NH	n-butyl	OCOOEt	5,6-dimethoxy-2-indolyl
NH	n-butyl	OCOOEt	5-methoxy-1-methyl-2-indolyl
NH	n-pentyl	OH	1-naphthyl
NH	n-pentyl	OH	2-naphthyl
NH	n-pentyl	OH	2-pyrrolyl
NH	n-pentyl	OH	3-pyrrolyl
NH	n-pentyl	OH	2-furyl
NH	n-pentyl	OH	3-furyl
NH	n-pentyl	OH	2-thienyl
NH	n-pentyl	OH	3-thienyl
NH	n-pentyl	OH	3-pyrazolyl
NH	n-pentyl	OH	4-pyrazolyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-pentyl	OH	2-imidazolyl
NH	n-pentyl	OH	4-imidazolyl
NH	n-pentyl	OH	2-oxazolyl
NH	n-pentyl	OH	4-oxazolyl
NH	n-pentyl	OH	5-oxazolyl
NH	n-pentyl	OH	2-thiazolyl
NH	n-pentyl	OH	4-thiazolyl
NH	n-pentyl	OH	5-thiazolyl
NH	n-pentyl	OH	2-pyrimidinyl
NH	n-pentyl	OH	4-pyrimidinyl
NH	n-pentyl	OH	5-pyrimidinyl
NH	n-pentyl	OH	2-indolyl
NH	n-pentyl	OH	3-indolyl
NH	n-pentyl	OH	5-indolyl
NH	n-pentyl	OH	6-indolyl
NH	n-pentyl	OH	5-benzimidazolyl
NH	n-pentyl	OH	2-benzofuryl
NH	n-pentyl	OH	3-indazolyl
NH	n-pentyl	OH	2-benzoxazolyl
NH	n-pentyl	OH	4-fluoro-1-naphthyl
NH	n-pentyl	OH	5-chloro-2-thienyl
NH	n-pentyl	OH	4-methyl-1-naphthyl
NH	n-pentyl	OH	1-methyl-2-pyrrolyl
NH	n-pentyl	OH	2-methyl-3-furyl
NH	n-pentyl	OH	5-methyl-2-thienyl
NH	n-pentyl	OH	4-methyl-5-imidazolyl
NH	n-pentyl	OH	1-methyl-3-indolyl
NH	n-pentyl	OH	2-methoxy-1-naphthyl
NH	n-pentyl	OH	3-methoxy-2-naphthyl
NH	n-pentyl	OH	6-ethoxy-2-naphthyl
NH	n-pentyl	OH	5-methoxy-3-indolyl
NH	n-pentyl	OH	1,4-dimethoxy-2-naphthyl
NH	n-pentyl	OH	5,6-dimethoxy-2-indolyl
NH	n-pentyl	OH	5-methoxy-1-methyl-2-indolyl
NH	n-pentyl	OCOOMe	1-naphthyl
NH	n-pentyl	OCOOMe	2-naphthyl
NH	n-pentyl	OCOOMe	2-pyrrolyl
NH	n-pentyl	OCOOMe	3-pyrrolyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-pentyl	OCOOMe	2-furyl
NH	n-pentyl	OCOOMe	3-furyl
NH	n-pentyl	OCOOMe	2-thienyl
NH	n-pentyl	OCOOMe	3-thienyl
NH	n-pentyl	OCOOMe	3-pyrazolyl
NH	n-pentyl	OCOOMe	4-pyrazolyl
NH	n-pentyl	OCOOMe	2-imidazolyl
NH	n-pentyl	OCOOMe	4-imidazolyl
NH	n-pentyl	OCOOMe	2-oxazolyl
NH	n-pentyl	OCOOMe	4-oxazolyl
NH	n-pentyl	OCOOMe	5-oxazolyl
NH	n-pentyl	OCOOMe	2-thiazolyl
NH	n-pentyl	OCOOMe	4-thiazolyl
NH	n-pentyl	OCOOMe	5-thiazolyl
NH	n-pentyl	OCOOMe	2-pyrimidinyl
NH	n-pentyl	OCOOMe	4-pyrimidinyl
NH	n-pentyl	OCOOMe	5-pyrimidinyl
NH	n-pentyl	OCOOMe	2-indolyl
NH	n-pentyl	OCOOMe	3-indolyl
NH	n-pentyl	OCOOMe	5-indolyl
NH	n-pentyl	OCOOMe	6-indolyl
NH	n-pentyl	OCOOMe	5-benzimidazolyl
NH	n-pentyl	OCOOMe	2-benzofuryl
NH	n-pentyl	OCOOMe	3-indazolyl
NH	n-pentyl	OCOOMe	2-benzoxazolyl
NH	n-pentyl	OCOOMe	4-fluoro-1-naphthyl
NH	n-pentyl	OCOOMe	5-chloro-2-thienyl
NH	n-pentyl	OCOOMe	4-methyl-1-naphthyl
NH	n-pentyl	OCOOMe	1-methyl-2-pyrrolyl
NH	n-pentyl	OCOOMe	2-methyl-3-furyl
NH	n-pentyl	OCOOMe	5-methyl-2-thienyl
NH	n-pentyl	OCOOMe	4-methyl-5-imidazolyl
NH	n-pentyl	OCOOMe	1-methyl-3-indolyl
NH	n-pentyl	OCOOMe	2-methoxy-1-naphthyl
NH	n-pentyl	OCOOMe	3-methoxy-2-naphthyl
NH	n-pentyl	OCOOMe	6-ethoxy-2-naphthyl
NH	n-pentyl	OCOOMe	5-methoxy-3-indolyl
NH	n-pentyl	OCOOMe	1,4-dimethoxy-2-naphthyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-pentyl	OCOOMe	5,6-dimethoxy-2-indolyl
NH	n-pentyl	OCOOMe	5-methoxy-1-methyl-2-indolyl
NH	n-pentyl	OCOOEt	1-naphthyl
NH	n-pentyl	OCOOEt	2-naphthyl
NH	n-pentyl	OCOOEt	2-pyrrolyl
NH	n-pentyl	OCOOEt	3-pyrrolyl
NH	n-pentyl	OCOOEt	2-furyl
NH	n-pentyl	OCOOEt	3-furyl
NH	n-pentyl	OCOOEt	2-thienyl
NH	n-pentyl	OCOOEt	3-thienyl
NH	n-pentyl	OCOOEt	3-pyrazolyl
NH	n-pentyl	OCOOEt	4-pyrazolyl
NH	n-pentyl	OCOOEt	2-imidazolyl
NH	n-pentyl	OCOOEt	4-imidazolyl
NH	n-pentyl	OCOOEt	2-oxazolyl
NH	n-pentyl	OCOOEt	4-oxazolyl
NH	n-pentyl	OCOOEt	5-oxazolyl
NH	n-pentyl	OCOOEt	2-thiazolyl
NH	n-pentyl	OCOOEt	4-thiazolyl
NH	n-pentyl	OCOOEt	5-thiazolyl
NH	n-pentyl	OCOOEt	2-pyrimidinyl
NH	n-pentyl	OCOOEt	4-pyrimidinyl
NH	n-pentyl	OCOOEt	5-pyrimidinyl
NH	n-pentyl	OCOOEt	2-indolyl
NH	n-pentyl	OCOOEt	3-indolyl
NH	n-pentyl	OCOOEt	5-indolyl
NH	n-pentyl	OCOOEt	6-indolyl
NH	n-pentyl	OCOOEt	5-benzimidazolyl
NH	n-pentyl	OCOOEt	2-benzofuryl
NH	n-pentyl	OCOOEt	3-indazolyl
NH	n-pentyl	OCOOEt	2-benzoxazolyl
NH	n-pentyl	OCOOEt	4-fluoro-1-naphthyl
NH	n-pentyl	OCOOEt	5-chloro-2-thienyl
NH	n-pentyl	OCOOEt	4-methyl-1-naphthyl
NH	n-pentyl	OCOOEt	1-methyl-2-pyrrolyl
NH	n-pentyl	OCOOEt	2-methyl-3-furyl
NH	n-pentyl	OCOOEt	5-methyl-2-thienyl
NH	n-pentyl	OCOOEt	4-methyl-5-imidazolyl

Table 1 (continued)

X	R^1	R^2	Y
NH	n-pentyl	OCOOEt	1-methyl-3-indolyl
NH	n-pentyl	OCOOEt	2-methoxy-1-naphthyl
NH	n-pentyl	OCOOEt	3-methoxy-2-naphthyl
NH	n-pentyl	OCOOEt	6-ethoxy-2-naphthyl
NH	n-pentyl	OCOOEt	5-methoxy-3-indolyl
NH	n-pentyl	OCOOEt	1,4-dimethoxy-2-naphthyl
NH	n-pentyl	OCOOEt	5,6-dimethoxy-2-indolyl
NH	n-pentyl	OCOOEt	5-methoxy-1-methyl-2-indolyl
O	propyl	OH	1-naphthyl
O	propyl	OH	2-naphthyl
O	propyl	OH	2-pyrrolyl
O	propyl	OH	3-pyrrolyl
O	propyl	OH	2-furyl
O	propyl	OH	3-furyl
O	propyl	OH	2-thienyl
O	propyl	OH	3-thienyl
O	propyl	OH	3-pyrazolyl
O	propyl	OH	4-pyrazolyl
O	propyl	OH	2-imidazolyl
O	propyl	OH	4-imidazolyl
O	propyl	OH	2-oxazolyl
O	propyl	OH	4-oxazolyl
O	propyl	OH	5-oxazolyl
O	propyl	OH	2-thiazolyl
O	propyl	OH	4-thiazolyl
O	propyl	OH	5-thiazolyl
O	propyl	OH	2-pyrimidinyl
O	propyl	OH	4-pyrimidinyl
O	propyl	OH	5-pyrimidinyl
O	propyl	OH	2-indolyl
O	propyl	OH	3-indolyl
O	propyl	OH	5-indolyl
O	propyl	OH	6-indolyl
O	propyl	OH	5-benzimidazolyl
O	propyl	OH	2-benzofuryl
O	propyl	OH	3-indazolyl
O	propyl	OH	2-benzoxazolyl
O	propyl	OH	4-fluoro-1-naphthyl

Table 1 (continued)

X	R^1	R^2	Y
O	propyl	OH	5-chloro-2-thienyl
O	propyl	OH	4-methyl-1-naphthyl
O	propyl	OH	1-methyl-2-pyrrolyl
O	propyl	OH	2-methyl-3-furyl
O	propyl	OH	5-methyl-2-thienyl
O	propyl	OH	4-methyl-5-imidazolyl
O	propyl	OH	1-methyl-3-indolyl
O	propyl	OH	2-methoxy-1-naphthyl
O	propyl	OH	3-methoxy-2-naphthyl
O	propyl	OH	6-ethoxy-2-naphthyl
O	propyl	OH	5-methoxy-3-indolyl
O	propyl	OH	1,4-dimethoxy-2-naphthyl
O	propyl	OH	5,6-dimethoxy-2-indolyl
O	propyl	OH	5-methoxy-1-methyl-2-indolyl
O	propyl	OCOOMe	1-naphthyl
O	propyl	OCOOMe	2-naphthyl
O	propyl	OCOOMe	2-pyrrolyl
O	propyl	OCOOMe	3-pyrrolyl
O	propyl	OCOOMe	2-furyl
O	propyl	OCOOMe	3-furyl
O	propyl	OCOOMe	2-thienyl
O	propyl	OCOOMe	3-thienyl
O	propyl	OCOOMe	3-pyrazolyl
O	propyl	OCOOMe	4-pyrazolyl
O	propyl	OCOOMe	2-imidazolyl
O	propyl	OCOOMe	4-imidazolyl
O	propyl	OCOOMe	2-oxazolyl
O	propyl	OCOOMe	4-oxazolyl
O	propyl	OCOOMe	5-oxazolyl
O	propyl	OCOOMe	2-thiazolyl
O	propyl	OCOOMe	4-thiazolyl
O	propyl	OCOOMe	5-thiazolyl
O	propyl	OCOOMe	2-pyrimidinyl
O	propyl	OCOOMe	4-pyrimidinyl
O	propyl	OCOOMe	5-pyrimidinyl
O	propyl	OCOOMe	2-indolyl
O	propyl	OCOOMe	3-indolyl
O	propyl	OCOOMe	5-indolyl

Table 1 (continued)

X	R^1	R^2	Y
O	propyl	OCOOMe	6-indolyl
O	propyl	OCOOMe	5-benzimidazolyl
O	propyl	OCOOMe	2-benzofuryl
O	propyl	OCOOMe	3-indazolyl
O	propyl	OCOOMe	2-benzoxazolyl
O	propyl	OCOOMe	4-fluoro-1-naphthyl
O	propyl	OCOOMe	5-chloro-2-thienyl
O	propyl	OCOOMe	4-methyl-1-naphthyl
O	propyl	OCOOMe	1-methyl-2-pyrrolyl
O	propyl	OCOOMe	2-methyl-3-furyl
O	propyl	OCOOMe	5-methyl-2-thienyl
O	propyl	OCOOMe	4-methyl-5-imidazolyl
O	propyl	OCOOMe	1-methyl-3-indolyl
O	propyl	OCOOMe	2-methoxy-1-naphthyl
O	propyl	OCOOMe	3-methoxy-2-naphthyl
O	propyl	OCOOMe	6-ethoxy-2-naphthyl
O	propyl	OCOOMe	5-methoxy-3-indolyl
O	propyl	OCOOMe	1,4-dimethoxy-2-naphthyl
O	propyl	OCOOMe	5,6-dimethoxy-2-indolyl
O	propyl	OCOOMe	5-methoxy-1-methyl-2-indolyl
O	propyl	OCOOEt	1-naphthyl
O	propyl	OCOOEt	2-naphthyl
O	propyl	OCOOEt	2-pyrrolyl
O	propyl	OCOOEt	3-pyrrolyl
O	propyl	OCOOEt	2-furyl
O	propyl	OCOOEt	3-furyl
O	propyl	OCOOEt	2-thienyl
O	propyl	OCOOEt	3-thienyl
O	propyl	OCOOEt	3-pyrazolyl
O	propyl	OCOOEt	4-pyrazolyl
O	propyl	OCOOEt	2-imidazolyl
O	propyl	OCOOEt	4-imidazolyl
O	propyl	OCOOEt	2-oxazolyl
O	propyl	OCOOEt	4-oxazolyl
O	propyl	OCOOEt	5-oxazolyl
O	propyl	OCOOEt	2-thiazolyl
O	propyl	OCOOEt	4-thiazolyl
O	propyl	OCOOEt	5-thiazolyl

Table 1 (continued)

X	R^1	R^2	Y
O	propyl	OCOOEt	2-pyrimidinyl
O	propyl	OCOOEt	4-pyrimidinyl
O	propyl	OCOOEt	5-pyrimidinyl
O	propyl	OCOOEt	2-indolyl
O	propyl	OCOOEt	3-indolyl
O	propyl	OCOOEt	5-indolyl
O	propyl	OCOOEt	6-indolyl
O	propyl	OCOOEt	5-benzimidazolyl
O	propyl	OCOOEt	2-benzofuryl
O	propyl	OCOOEt	3-indazolyl
O	propyl	OCOOEt	2-benzoxazolyl
O	propyl	OCOOEt	4-fluoro-1-naphthyl
O	propyl	OCOOEt	5-chloro-2-thienyl
O	propyl	OCOOEt	4-methyl-1-naphthyl
O	propyl	OCOOEt	1-methyl-2-pyrrolyl
O	propyl	OCOOEt	2-methyl-3-furyl
O	propyl	OCOOEt	5-methyl-2-thienyl
O	propyl	OCOOEt	4-methyl-5-imidazolyl
O	propyl	OCOOEt	1-methyl-3-indolyl
O	propyl	OCOOEt	2-methoxy-1-naphthyl
O	propyl	OCOOEt	3-methoxy-2-naphthyl
O	propyl	OCOOEt	6-ethoxy-2-naphthyl
O	propyl	OCOOEt	5-methoxy-3-indolyl
O	propyl	OCOOEt	1,4-dimethoxy-2-naphthyl
O	propyl	OCOOEt	5,6-dimethoxy-2-indolyl
O	propyl	OCOOEt	5-methoxy-1-methyl-2-indolyl
O	n-butyl	OH	1-naphthyl
O	n-butyl	OH	2-naphthyl
O	n-butyl	OH	2-pyrrolyl
O	n-butyl	OH	3-pyrrolyl
O	n-butyl	OH	2-furyl
O	n-butyl	OH	3-furyl
O	n-butyl	OH	2-thienyl
O	n-butyl	OH	3-thienyl
O	n-butyl	OH	3-pyrazolyl
O	n-butyl	OH	4-pyrazolyl
O	n-butyl	OH	2-imidazolyl
O	n-butyl	OH	4-imidazolyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-butyl	OH	2-oxazolyl
O	n-butyl	OH	4-oxazolyl
O	n-butyl	OH	5-oxazolyl
O	n-butyl	OH	2-thiazolyl
O	n-butyl	OH	4-thiazolyl
O	n-butyl	OH	5-thiazolyl
O	n-butyl	OH	2-pyrimidinyl
O	n-butyl	OH -	4-pyrimidinyl
O	n-butyl	OH	5-pyrimidinyl
O	n-butyl	OH	2-indolyl
O	n-butyl	OH	3-indolyl
O	n-butyl	OH	5-indolyl
O	n-butyl	OH	6-indolyl
O	n-butyl	OH	5-benzimidazolyl
O	n-butyl	OH	2-benzofuryl
O	n-butyl	OH	3-indazolyl
O	n-butyl	OH	2-benzoxazolyl
O	n-butyl	OH	4-fluoro-1-naphthyl
O	n-butyl	OH	5-chloro-2-thienyl
O	n-butyl	OH	4-methyl-1-naphthyl
O	n-butyl	OH	1-methyl-2-pyrrolyl
O	n-butyl	OH	2-methyl-3-furyl
O	n-butyl	OH	5-methyl-2-thienyl
O	n-butyl	OH	4-methyl-5-imidazolyl
O	n-butyl	OH	1-methyl-3-indolyl
O	n-butyl	OH	2-methoxy-1-naphthyl
O	n-butyl	OH	3-methoxy-2-naphthyl
O	n-butyl	OH	6-ethoxy-2-naphthyl
O	n-butyl	OH	5-methoxy-3-indolyl
O	n-butyl	OH	1,4-dimethoxy-2-naphthyl
O	n-butyl	OH	5,6-dimethoxy-2-indolyl
O	n-butyl	OH	5-methoxy-1-methyl-2-indolyl
O	n-butyl	OCOOMe	1-naphthyl
O	n-butyl	OCOOMe	2-naphthyl
O	n-butyl	OCOOMe	2-pyrrolyl
O	n-butyl	OCOOMe	3-pyrrolyl
O	n-butyl	OCOOMe	2-furyl
O	n-butyl	OCOOMe	3-furyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-butyl	OCOOMe	2-thienyl
O	n-butyl	OCOOMe	3-thienyl
O	n-butyl	OCOOMe	3-pyrazolyl
O	n-butyl	OCOOMe	4-pyrazolyl
O	n-butyl	OCOOMe	2-imidazolyl
O	n-butyl	OCOOMe	4-imidazolyl
O	n-butyl	OCOOMe	2-oxazolyl
O	n-butyl	OCOOMe	4-oxazolyl
O	n-butyl	OCOOMe	5-oxazolyl
O	n-butyl	OCOOMe	2-thiazolyl
O	n-butyl	OCOOMe	4-thiazolyl
O	n-butyl	OCOOMe	5-thiazolyl
O	n-butyl	OCOOMe	2-pyrimidinyl
O	n-butyl	OCOOMe	4-pyrimidinyl
O	n-butyl	OCOOMe	5-pyrimidinyl
O	n-butyl	OCOOMe	2-indolyl
O	n-butyl	OCOOMe	3-indolyl
O	n-butyl	OCOOMe	5-indolyl
O	n-butyl	OCOOMe	6-indolyl
O	n-butyl	OCOOMe	5-benzimidazolyl
O	n-butyl	OCOOMe	2-benzofuryl
O	n-butyl	OCOOMe	3-indazolyl
O	n-butyl	OCOOMe	2-benzoxazolyl
O	n-butyl	OCOOMe	4-fluoro-1-naphthyl
O	n-butyl	OCOOMe	5-chloro-2-thienyl
O	n-butyl	OCOOMe	4-methyl-1-naphthyl
O	n-butyl	OCOOMe	1-methyl-2-pyrrolyl
O	n-butyl	OCOOMe	2-methyl-3-furyl
O	n-butyl	OCOOMe	5-methyl-2-thienyl
O	n-butyl	OCOOMe	4-methyl-5-imidazolyl
O	n-butyl	OCOOMe	1-methyl-3-indolyl
O	n-butyl	OCOOMe	2-methoxy-1-naphthyl
O	n-butyl	OCOOMe	3-methoxy-2-naphthyl
O	n-butyl	OCOOMe	6-ethoxy-2-naphthyl
O	n-butyl	OCOOMe	5-methoxy-3-indolyl
O	n-butyl	OCOOMe	1,4-dimethoxy-2-naphthyl
O	n-butyl	OCOOMe	5,6-dimethoxy-2-indolyl
O	n-butyl	OCOOMe	5-methoxy-1-methyl-2-indolyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-butyl	OCOOEt	1-naphthyl
O	n-butyl	OCOOEt	2-naphthyl
O	n-butyl	OCOOEt	2-pyrrolyl
O	n-butyl	OCOOEt	3-pyrrolyl
O	n-butyl	OCOOEt	2-furyl
O	n-butyl	OCOOEt	3-furyl
O	n-butyl	OCOOEt	2-thienyl
O	n-butyl	OCOOEt	3-thienyl
O	n-butyl	OCOOEt	3-pyrazolyl
O	n-butyl	OCOOEt	4-pyrazolyl
O	n-butyl	OCOOEt	2-imidazolyl
O	n-butyl	OCOOEt	4-imidazolyl
O	n-butyl	OCOOEt	2-oxazolyl
O	n-butyl	OCOOEt	4-oxazolyl
O	n-butyl	OCOOEt	5-oxazolyl
O	n-butyl	OCOOEt	2-thiazolyl
O	n-butyl	OCOOEt	4-thiazolyl
O	n-butyl	OCOOEt	5-thiazolyl
O	n-butyl	OCOOEt	2-pyrimidinyl
O	n-butyl	OCOOEt	4-pyrimidinyl
O	n-butyl	OCOOEt	5-pyrimidinyl
O	n-butyl	OCOOEt	2-indolyl
O	n-butyl	OCOOEt	3-indolyl
O	n-butyl	OCOOEt	5-indolyl
O	n-butyl	OCOOEt	6-indolyl
O	n-butyl	OCOOEt	5-benzimidazolyl
O	n-butyl	OCOOEt	2-benzofuryl
O	n-butyl	OCOOEt	3-indazolyl
O	n-butyl	OCOOEt	2-benzoxazolyl
O	n-butyl	OCOOEt	4-fluoro-1-naphthyl
O	n-butyl	OCOOEt	5-chloro-2-thienyl
O	n-butyl	OCOOEt	4-methyl-1-naphthyl
O	n-butyl	OCOOEt	1-methyl-2-pyrrolyl
O	n-butyl	OCOOEt	2-methyl-3-furyl
O	n-butyl	OCOOEt	5-methyl-2-thienyl
O	n-butyl	OCOOEt	4-methyl-5-imidazolyl
O	n-butyl	OCOOEt	1-methyl-3-indolyl
O	n-butyl	OCOOEt	2-methoxy-1-naphthyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-butyl	OCOOEt	3-methoxy-2-naphthyl
O	n-butyl	OCOOEt	6-ethoxy-2-naphthyl
O	n-butyl	OCOOEt	5-methoxy-3-indolyl
O	n-butyl	OCOOEt	1,4-dimethoxy-2-naphthyl
O	n-butyl	OCOOEt	5,6-dimethoxy-2-indolyl
O	n-butyl	OCOOEt	5-methoxy-1-methyl-2-indolyl
O	n-pentyl	OH	1-naphthyl
O	n-pentyl	OH	2-naphthyl
O	n-pentyl	OH	2-pyrrolyl
O	n-pentyl	OH	3-pyrrolyl
O	n-pentyl	OH	2-furyl
O	n-pentyl	OH	3-furyl
O	n-pentyl	OH	2-thienyl
O	n-pentyl	OH	3-thienyl
O	n-pentyl	OH	3-pyrazolyl
O	n-pentyl	OH	4-pyrazolyl
O	n-pentyl	OH	2-imidazolyl
O	n-pentyl	OH	4-imidazolyl
O	n-pentyl	OH	2-oxazolyl
O	n-pentyl	OH	4-oxazolyl
O	n-pentyl	OH	5-oxazolyl
O	n-pentyl	OH	2-thiazolyl
O	n-pentyl	OH	4-thiazolyl
O	n-pentyl	OH	5-thiazolyl
O	n-pentyl	OH	2-pyrimidinyl
O	n-pentyl	OH	4-pyrimidinyl
O	n-pentyl	OH	5-pyrimidinyl
O	n-pentyl	OH	2-indolyl
O	n-pentyl	OH	3-indolyl
O	n-pentyl	OH	5-indolyl
O	n-pentyl	OH	6-indolyl
O	n-pentyl	OH	5-benzimidazolyl
O	n-pentyl	OH	2-benzofuryl
O	n-pentyl	OH	3-indazolyl
O	n-pentyl	OH	2-benzoxazolyl
O	n-pentyl	OH	4-fluoro-1-naphthyl
O	n-pentyl	OH	5-chloro-2-thienyl
O	n-pentyl	OH	4-methyl-1-naphthyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-pentyl	OH	1-methyl-2-pyrrolyl
O	n-pentyl	OH	2-methyl-3-furyl
O	n-pentyl	OH	5-methyl-2-thienyl
O	n-pentyl	OH	4-methyl-5-imidazolyl
O	n-pentyl	OH	1-methyl-3-indolyl
O	n-pentyl	OH	2-methoxy-1-naphthyl
O	n-pentyl	OH	3-methoxy-2-naphthyl
O	n-pentyl	OH	6-ethoxy-2-naphthyl
O	n-pentyl	OH	5-methoxy-3-indolyl
O	n-pentyl	OH	1,4-dimethoxy-2-naphthyl
O	n-pentyl	OH	5,6-dimethoxy-2-indolyl
O	n-pentyl	OH	5-methoxy-1-methyl-2-indolyl
O	n-pentyl	OCOOMe	1-naphthyl
O	n-pentyl	OCOOMe	2-naphthyl
O	n-pentyl	OCOOMe	2-pyrrolyl
O	n-pentyl	OCOOMe	3-pyrrolyl
O	n-pentyl	OCOOMe	2-furyl
O	n-pentyl	OCOOMe	3-furyl
O	n-pentyl	OCOOMe	2-thienyl
O	n-pentyl	OCOOMe	3-thienyl
O	n-pentyl	OCOOMe	3-pyrazolyl
O	n-pentyl	OCOOMe	4-pyrazolyl
O	n-pentyl	OCOOMe	2-imidazolyl
O	n-pentyl	OCOOMe	4-imidazolyl
O	n-pentyl	OCOOMe	2-oxazolyl
O	n-pentyl	OCOOMe	4-oxazolyl
O	n-pentyl	OCOOMe	5-oxazolyl
O	n-pentyl	OCOOMe	2-thiazolyl
O	n-pentyl	OCOOMe	4-thiazolyl
O	n-pentyl	OCOOMe	5-thiazolyl
O	n-pentyl	OCOOMe	2-pyrimidinyl
O	n-pentyl	OCOOMe	4-pyrimidinyl
O	n-pentyl	OCOOMe	5-pyrimidinyl
O	n-pentyl	OCOOMe	2-indolyl
O	n-pentyl	OCOOMe	3-indolyl
O	n-pentyl	OCOOMe	5-indolyl
O	n-pentyl	OCOOMe	6-indolyl
O	n-pentyl	OCOOMe	5-benzimidazolyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-pentyl	OCOOMe	2-benzofuryl
O	n-pentyl	OCOOMe	3-indazolyl
O	n-pentyl	OCOOMe	2-benzoxazolyl
O	n-pentyl	OCOOMe	4-fluoro-1-naphthyl
O	n-pentyl	OCOOMe	5-chloro-2-thienyl
O	n-pentyl	OCOOMe	4-methyl-1-naphthyl
O	n-pentyl	OCOOMe	1-methyl-2-pyrrolyl
O	n-pentyl	OCOOMe	2-methyl-3-furyl
O	n-pentyl	OCOOMe	5-methyl-2-thienyl
O	n-pentyl	OCOOMe	4-methyl-5-imidazolyl
O	n-pentyl	OCOOMe	1-methyl-3-indolyl
O	n-pentyl	OCOOMe	2-methoxy-1-naphthyl
O	n-pentyl	OCOOMe	3-methoxy-2-naphthyl
O	n-pentyl	OCOOMe	6-ethoxy-2-naphthyl
O	n-pentyl	OCOOMe	5-methoxy-3-indolyl
O	n-pentyl	OCOOMe	1,4-dimethoxy-2-naphthyl
O	n-pentyl	OCOOMe	5,6-dimethoxy-2-indolyl
O	n-pentyl	OCOOMe	5-methoxy-1-methyl-2-indolyl
O	n-pentyl	OCOOEt	1-naphthyl
O	n-pentyl	OCOOEt	2-naphthyl
O	n-pentyl	OCOOEt	2-pyrrolyl
O	n-pentyl	OCOOEt	3-pyrrolyl
O	n-pentyl	OCOOEt	2-furyl
O	n-pentyl	OCOOEt	3-furyl
O	n-pentyl	OCOOEt	2-thienyl
O	n-pentyl	OCOOEt	3-thienyl
O	n-pentyl	OCOOEt	3-pyrazolyl
O	n-pentyl	OCOOEt	4-pyrazolyl
O	n-pentyl	OCOOEt	2-imidazolyl
O	n-pentyl	OCOOEt	4-imidazolyl
O	n-pentyl	OCOOEt	2-oxazolyl
O	n-pentyl	OCOOEt	4-oxazolyl
O	n-pentyl	OCOOEt	5-oxazolyl
O	n-pentyl	OCOOEt	2-thiazolyl
O	n-pentyl	OCOOEt	4-thiazolyl
O	n-pentyl	OCOOEt	5-thiazolyl
O	n-pentyl	OCOOEt	2-pyrimidinyl
O	n-pentyl	OCOOEt	4-pyrimidinyl

Table 1 (continued)

X	R^1	R^2	Y
O	n-pentyl	OCOOEt	5-pyrimidinyl
O	n-pentyl	OCOOEt	2-indolyl
O	n-pentyl	OCOOEt	3-indolyl
O	n-pentyl	OCOOEt	5-indolyl
O	n-pentyl	OCOOEt	6-indolyl
O	n-pentyl	OCOOEt	5-benzimidazolyl
O	n-pentyl	OCOOEt	2-benzofuryl
O	n-pentyl	OCOOEt	3-indazolyl
O	n-pentyl	OCOOEt	2-benzoxazolyl
O	n-pentyl	OCOOEt	4-fluoro-1-naphthyl
O	n-pentyl	OCOOEt	5-chloro-2-thienyl
O	n-pentyl	OCOOEt	4-methyl-1-naphthyl
O	n-pentyl	OCOOEt	1-methyl-2-pyrrolyl
O	n-pentyl	OCOOEt	2-methyl-3-furyl
O	n-pentyl	OCOOEt	5-methyl-2-thienyl
O	n-pentyl	OCOOEt	4-methyl-5-imidazolyl
O	n-pentyl	OCOOEt	1-methyl-3-indolyl
O	n-pentyl	OCOOEt	2-methoxy-1-naphthyl
O	n-pentyl	OCOOEt	3-methoxy-2-naphthyl
O	n-pentyl	OCOOEt	6-ethoxy-2-naphthyl
O	n-pentyl	OCOOEt	5-methoxy-3-indolyl
O	n-pentyl	OCOOEt	1,4-dimethoxy-2-naphthyl
O	n-pentyl	OCOOEt	5,6-dimethoxy-2-indolyl
O	n-pentyl	OCOOEt	5-methoxy-1-methyl-2-indolyl
S	propyl	OH	1-naphthyl
S	propyl	OH	2-naphthyl
S	propyl	OH	2-pyrrolyl
S	propyl	OH	3-pyrrolyl
S	propyl	OH	2-furyl
S	propyl	OH	3-furyl
S	propyl	OH	2-thienyl
S	propyl	OH	3-thienyl
S	propyl	OH	3-pyrazolyl
S	propyl	OH	4-pyrazolyl
S	propyl	OH	2-imidazolyl
S	propyl	OH	4-imidazolyl
S	propyl	OH	2-oxazolyl
S	propyl	OH	4-oxazolyl

Table 1 (continued)

X	R^1	R^2	Y
S	propyl	OH	5-oxazolyl
S	propyl	OH	2-thiazolyl
S	propyl	OH	4-thiazolyl
S	propyl	OH	5-thiazolyl
S	propyl	OH	2-pyrimidinyl
S	propyl	OH	4-pyrimidinyl
S	propyl	OH	5-pyrimidinyl
S	propyl	OH	2-indolyl
S	propyl	OH	3-indolyl
S	propyl	OH	5-indolyl
S	propyl	OH	6-indolyl
S	propyl	OH	5-benzimidazolyl
S	propyl	OH	2-benzofuryl
S	propyl	OH	3-indazolyl
S	propyl	OH	2-benzoxazolyl
S	propyl	OH	4-fluoro-1-naphthyl
S	propyl	OH	5-chloro-2-thienyl
S	propyl	OH	4-methyl-1-naphthyl
S	propyl	OH	1-methyl-2-pyrrolyl
S	propyl	OH	2-methyl-3-furyl
S	propyl	OH	5-methyl-2-thienyl
S	propyl	OH	4-methyl-5-imidazolyl
S	propyl	OH	1-methyl-3-indolyl
S	propyl	OH	2-methoxy-1-naphthyl
S	propyl	OH	3-methoxy-2-naphthyl
S	propyl	OH	6-ethoxy-2-naphthyl
S	propyl	OH	5-methoxy-3-indolyl
S	propyl	OH	1,4-dimethoxy-2-naphthyl
S	propyl	OH	5,6-dimethoxy-2-indolyl
S	propyl	OH	5-methoxy-1-methyl-2-indolyl
S	propyl	OCOOMe	1-naphthyl
S	propyl	OCOOMe	2-naphthyl
S	propyl	OCOOMe	2-pyrrolyl
S	propyl	OCOOMe	3-pyrrolyl
S	propyl	OCOOMe	2-furyl
S	propyl	OCOOMe	3-furyl
S	propyl	OCOOMe	2-thienyl
S	propyl	OCOOMe	3-thienyl

Table 1 (continued)

X	R^1	R^2	Y
S	propyl	OCOOMe	3-pyrazolyl
S	propyl	OCOOMe	4-pyrazolyl
S	propyl	OCOOMe	2-imidazolyl
S	propyl	OCOOMe	4-imidazolyl
S	propyl	OCOOMe	2-oxazolyl
S	propyl	OCOOMe	4-oxazolyl
S	propyl	OCOOMe	5-oxazolyl
S	propyl	OCOOMe	2-thiazolyl
S	propyl	OCOOMe	4-thiazolyl
S	propyl	OCOOMe	5-thiazolyl
S	propyl	OCOOMe	2-pyrimidinyl
S	propyl	OCOOMe	4-pyrimidinyl
S	propyl	OCOOMe	5-pyrimidinyl
S	propyl	OCOOMe	2-indolyl
S	propyl	OCOOMe	3-indolyl
S	propyl	OCOOMe	5-indolyl
S	propyl	OCOOMe	6-indolyl
S	propyl	OCOOMe	5-benzimidazolyl
S	propyl	OCOOMe	2-benzofuryl
S	propyl	OCOOMe	3-indazolyl
S	propyl	OCOOMe	2-benzoxazolyl
S	propyl	OCOOMe	4-fluoro-1-naphthyl
S	propyl	OCOOMe	5-chloro-2-thienyl
S	propyl	OCOOMe	4-methyl-1-naphthyl
S	propyl	OCOOMe	1-methyl-2-pyrrolyl
S	propyl	OCOOMe	2-methyl-3-furyl
S	propyl	OCOOMe	5-methyl-2-thienyl
S	propyl	OCOOMe	4-methyl-5-imidazolyl
S	propyl	OCOOMe	1-methyl-3-indolyl
S	propyl	OCOOMe	2-methoxy-1-naphthyl
S	propyl	OCOOMe	3-methoxy-2-naphthyl
S	propyl	OCOOMe	6-ethoxy-2-naphthyl
S	propyl	OCOOMe	5-methoxy-3-indolyl
S	propyl	OCOOMe	1,4-dimethoxy-2-naphthyl
S	propyl	OCOOMe	5,6-dimethoxy-2-indolyl
S	propyl	OCOOMe	5-methoxy-1-methyl-2-indolyl
S	propyl	OCOOEt	1-naphthyl
S	propyl	OCOOEt	2-naphthyl

Table 1 (continued)

X	R^1	R^2	Y
S	propyl	OCOOEt	2-pyrrolyl
S	propyl	OCOOEt	3-pyrrolyl
S	propyl	OCOOEt	2-furyl
S	propyl	OCOOEt	3-furyl
S	propyl	OCOOEt	2-thienyl
S	propyl	OCOOEt	3-thienyl
S	propyl	OCOOEt	3-pyrazolyl
S	propyl	OCOOEt	4-pyrazolyl
S	propyl	OCOOEt	2-imidazolyl
S	propyl	OCOOEt	4-imidazolyl
S	propyl	OCOOEt	2-oxazolyl
S	propyl	OCOOEt	4-oxazolyl
S	propyl	OCOOEt	5-oxazolyl
S	propyl	OCOOEt	2-thiazolyl
S	propyl	OCOOEt	4-thiazolyl
S	propyl	OCOOEt	5-thiazolyl
S	propyl	OCOOEt	2-pyrimidinyl
S	propyl	OCOOEt	4-pyrimidinyl
S	propyl	OCOOEt	5-pyrimidinyl
S	propyl	OCOOEt	2-indolyl
S	propyl	OCOOEt	3-indolyl
S	propyl	OCOOEt	5-indolyl
S	propyl	OCOOEt	6-indolyl
S	propyl	OCOOEt	5-benzimidazolyl
S	propyl	OCOOEt	2-benzofuryl
S	propyl	OCOOEt	3-indazolyl
S	propyl	OCOOEt	2-benzoxazolyl
S	propyl	OCOOEt	4-fluoro-1-naphthyl
S	propyl	OCOOEt	5-chloro-2-thienyl
S	propyl	OCOOEt	4-methyl-1-naphthyl
S	propyl	OCOOEt	1-methyl-2-pyrrolyl
S	propyl	OCOOEt	2-methyl-3-furyl
S	propyl	OCOOEt	5-methyl-2-thienyl
S	propyl	OCOOEt	4-methyl-5-imidazolyl
S	propyl	OCOOEt	1-methyl-3-indolyl
S	propyl	OCOOEt	2-methoxy-1-naphthyl
S	propyl	OCOOEt	3-methoxy-2-naphthyl
S	propyl	OCOOEt	6-ethoxy-2-naphthyl

Table 1 (continued)

X	R^1	R^2	Y
S	propyl	OCOOEt	5-methoxy-3-indolyl
S	propyl	OCOOEt	1,4-dimethoxy-2-naphthyl
S	propyl	OCOOEt	5,6-dimethoxy-2-indolyl
S	propyl	OCOOEt	5-methoxy-1-methyl-Z-indolyl
S	n-butyl	OH	1-naphthyl
S	n-butyl	OH	2-naphthyl
S	n-butyl	OH	2-pyrrolyl
S	n-butyl	OH	3-pyrrolyl
S	n-butyl	OH	2-furyl
S	n-butyl	OH	3-furyl
S	n-butyl	OH	2-thienyl
S	n-butyl	OH	3-thienyl
S	n-butyl	OH	3-pyrazolyl
S	n-butyl	OH	4-pyrazolyl
S	n-butyl	OH	2-imidazolyl
S	n-butyl	OH	4-imidazolyl
S	n-butyl	OH	2-oxazolyl
S	n-butyl	OH	4-oxazolyl
S	n-butyl	OH	5-oxazolyl
S	n-butyl	OH	2-thiazolyl
S	n-butyl	OH	4-thiazolyl
S	n-butyl	OH	5-thiazolyl
S	n-butyl	OH	2-pyrimidinyl
S	n-butyl	OH	4-pyrimidinyl
S	n-butyl	OH	5-pyrimidinyl
S	n-butyl	OH	2-indolyl
S	n-butyl	OH	3-indolyl
S	n-butyl	OH	5-indolyl
S	n-butyl	OH	6-indolyl
S	n-butyl	OH	5-benzimidazolyl
S	n-butyl	OH	2-benzofuryl
S	n-butyl	OH	3-indazolyl
S	n-butyl	OH	2-benzoxazolyl
S	n-butyl	OH	4-fluoro-1-naphthyl
S	n-butyl	OH	5-chloro-2-thienyl
S	n-butyl	OH	4-methyl-1-naphthyl
S	n-butyl	OH	1-methyl-2-pyrrolyl
S	n-butyl	OH	2-methyl-3-furyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-butyl	OH	5-methyl-2-thienyl
S	n-butyl	OH	4-methyl-5-imidazolyl
S	n-butyl	OH	1-methyl-3-indolyl
S	n-butyl	OH	2-methoxy-1-naphthyl
S	n-butyl	OH	3-methoxy-2-naphthyl
S	n-butyl	OH	6-ethoxy-2-naphthyl
S	n-butyl	OH	5-methoxy-3-indolyl
S	n-butyl	OH	1,4-dimethoxy-2-naphthyl
S	n-butyl	OH	5,6-dimethoxy-2-indolyl
S	n-butyl	OH	5-methoxy-1-methyl-2-indolyl
S	n-butyl	OCOOMe	1-naphthyl
S	n-butyl	OCOOMe	2-naphthyl
S	n-butyl	OCOOMe	2-pyrrolyl
S	n-butyl	OCOOMe	3-pyrrolyl
S	n-butyl	OCOOMe	2-furyl
S	n-butyl	OCOOMe	3-furyl
S	n-butyl	OCOOMe	2-thienyl
S	n-butyl	OCOOMe	3-thienyl
S	n-butyl	OCOOMe	3-pyrazolyl
S	n-butyl	OCOOMe	4-pyrazolyl
S	n-butyl	OCOOMe	2-imidazolyl
S	n-butyl	OCOOMe	4-imidazolyl
S	n-butyl	OCOOMe	2-oxazolyl
S	n-butyl	OCOOMe	4-oxazolyl
S	n-butyl	OCOOMe	5-oxazolyl
S	n-butyl	OCOOMe	2-thiazolyl
S	n-butyl	OCOOMe	4-thiazolyl
S	n-butyl	OCOOMe	5-thiazolyl
S	n-butyl	OCOOMe	2-pyrimidinyl
S	n-butyl	OCOOMe	4-pyrimidinyl
S	n-butyl	OCOOMe	5-pyrimidinyl
S	n-butyl	OCOOMe	2-indolyl
S	n-butyl	OCOOMe	3-indolyl
S	n-butyl	OCOOMe	5-indolyl
S	n-butyl	OCOOMe	6-indolyl
S	n-butyl	OCOOMe	5-benzimidazolyl
S	n-butyl	OCOOMe	2-benzofuryl
S	n-butyl	OCOOMe	3-indazolyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-butyl	OCOOMe	2-benzoxazolyl
S	n-butyl	OCOOMe	4-fluoro-1-naphthyl
S	n-butyl	OCOOMe	5-chloro-2-thienyl
S	n-butyl	OCOOMe	4-methyl-1-naphthyl
S	n-butyl	OCOOMe	1-methyl-2-pyrrolyl
S	n-butyl	OCOOMe	2-methyl-3-furyl
S	n-butyl	OCOOMe	5-methyl-2-thienyl
S	n-butyl	OCOOMe	4-methyl-5-imidazolyl
S	n-butyl	OCOOMe	1-methyl-3-indolyl
S	n-butyl	OCOOMe	2-methoxy-1-naphthyl
S	n-butyl	OCOOMe	3-methoxy-2-naphthyl
S	n-butyl	OCOOMe	6-ethoxy-2-naphthyl
S	n-butyl	OCOOMe	5-methoxy-3-indolyl
S	n-butyl	OCOOMe	1,4-dimethoxy-2-naphthyl
S	n-butyl	OCOOMe	5,6-dimethoxy-2-indolyl
S	n-butyl	OCOOMe	5-methoxy-1-methyl-2-indolyl
S	n-butyl	OCOOEt	1-naphthyl
S	n-butyl	OCOOEt	2-naphthyl
S	n-butyl	OCOOEt	2-pyrrolyl
S	n-butyl	OCOOEt	3-pyrrolyl
S	n-butyl	OCOOEt	2-furyl
S	n-butyl	OCOOEt	3-furyl
S	n-butyl	OCOOEt	2-thienyl
S	n-butyl	OCOOEt	3-thienyl
S	n-butyl	OCOOEt	3-pyrazolyl
S	n-butyl	OCOOEt	4-pyrazolyl
S	n-butyl	OCOOEt	2-imidazolyl
S	n-butyl	OCOOEt	4-imidazolyl
S	n-butyl	OCOOEt	2-oxazolyl
S	n-butyl	OCOOEt	4-oxazolyl
S	n-butyl	OCOOEt	5-oxazolyl
S	n-butyl	OCOOEt	2-thiazolyl
S	n-butyl	OCOOEt	4-thiazolyl
S	n-butyl	OCOOEt	5-thiazolyl
S	n-butyl	OCOOEt	2-pyrimidinyl
S	n-butyl	OCOOEt	4-pyrimidinyl
S	n-butyl	OCOOEt	5-pyrimidinyl
S	n-butyl	OCOOEt	2-indolyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-butyl	OCOOEt	3-indolyl
S	n-butyl	OCOOEt	5-indolyl
S	n-butyl	OCOOEt	6-indolyl
S	n-butyl	OCOOEt	5-benzimidazolyl
S	n-butyl	OCOOEt	2-benzofuryl
S	n-butyl	OCOOEt	3-indazolyl
S	n-butyl	OCOOEt	2-benzoxazolyl
S	n-butyl	OCOOEt	4-fluoro-1-naphthyl
S	n-butyl	OCOOEt	5-chloro-2-thienyl
S	n-butyl	OCOOEt	4-methyl-1-naphthyl
S	n-butyl	OCOOEt	1-methyl-2-pyrrolyl
S	n-butyl	OCOOEt	2-methyl-3-furyl
S	n-butyl	OCOOEt	5-methyl-2-thienyl
S	n-butyl	OCOOEt	4-methyl-5-imidazolyl
S	n-butyl	OCOOEt	1-methyl-3-indolyl
S	n-butyl	OCOOEt	2-methoxy-1-naphthyl
S	n-butyl	OCOOEt	3-methoxy-2-naphthyl
S	n-butyl	OCOOEt	6-ethoxy-2-naphthyl
S	n-butyl .	OCOOEt	5-methoxy-3-indolyl
S	n-butyl	OCOOEt	1,4-dimethoxy-2-naphthyl
S	n-butyl	OCOOEt	5,6-dimethoxy-2-indolyl
S	n-butyl	OCOOEt	5-methoxy-1-methyl-2-indolyl
S	n-pentyl	OH	1-naphthyl
S	n-pentyl	OH	2-naphthyl
S	n-pentyl	OH	2-pyrrolyl
S	n-pentyl	OH	3-pyrrolyl
S	n-pentyl	OH	2-furyl
S	n-pentyl	OH	3-furyl
S	n-pentyl	OH	2-thienyl
S	n-pentyl	OH	3-thienyl
S	n-pentyl	OH	3-pyrazolyl
S	n-pentyl	OH	4-pyrazolyl
S	n-pentyl	OH	2-imidazolyl
S	n-pentyl	OH	4-imidazolyl
S	n-pentyl	OH	2-oxazolyl
S	n-pentyl	OH	4-oxazolyl
S	n-pentyl	OH	5-oxazolyl
S	n-pentyl	OH	2-thiazolyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-pentyl	OH	4-thiazolyl
S	n-pentyl	OH	5-thiazolyl
S	n-pentyl	OH	2-pyrimidinyl
S	n-pentyl	OH	4-pyrimidinyl
S	n-pentyl	OH	5-pyrimidinyl
S	n-pentyl	OH	2-indolyl
S	n-pentyl	OH	3-indolyl
S	n-pentyl	OH	5-indolyl
S	n-pentyl	OH	6-indolyl
S	n-pentyl	OH	5-benzimidazolyl
S	n-pentyl	OH	2-benzofuryl
S	n-pentyl	OH	3-indazolyl
S	n-pentyl	OH	2-benzoxazolyl
S	n-pentyl	OH	4-fluoro-1-naphthyl
S	n-pentyl	OH	5-chloro-2-thienyl
S	n-pentyl	OH	4-methyl-1-naphthyl
S	n-pentyl	OH	1-methyl-2-pyrrolyl
S	n-pentyl	OH	2-methyl-3-furyl
S	n-pentyl	OH	5-methyl-2-thienyl
S	n-pentyl	OH	4-methyl-5-imidazolyl
S	n-pentyl	OH	1-methyl-3-indolyl
S	n-pentyl	OH	2-methoxy-1-naphthyl
S	n-pentyl	OH	3-methoxy-2-naphthyl
S	n-pentyl	OH	6-ethoxy-2-naphthyl
S	n-pentyl	OH	5-methoxy-3-indolyl
S	n-pentyl	OH	1,4-dimethoxy-2-naphthyl
S	n-pentyl	OH	5,6-dimethoxy-2-indolyl
S	n-pentyl	OH	5-methoxy-1-methyl-2-indolyl
S	n-pentyl	OCOOMe	1-naphthyl
S	n-pentyl	OCOOMe	2-naphthyl
S	n-pentyl	OCOOMe	2-pyrrolyl
S	n-pentyl	OCOOMe	3-pyrrolyl
S	n-pentyl	OCOOMe	2-furyl
S	n-pentyl	OCOOMe	3-furyl
S	n-pentyl	OCOOMe	2-thienyl
S	n-pentyl	OCOOMe	3-thienyl
S	n-pentyl	OCOOMe	3-pyrazolyl
S	n-pentyl	OCOOMe	4-pyrazolyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-pentyl	OCOOMe	2-imidazolyl
S	n-pentyl	OCOOMe	4-imidazolyl
S	n-pentyl	OCOOMe	2-oxazolyl
S	n-pentyl	OCOOMe	4-oxazolyl
S	n-pentyl	OCOOMe	5-oxazolyl
S	n-pentyl	OCOOMe	2-thiazolyl
S	n-pentyl	OCOOMe	4-thiazolyl
S	n-pentyl	OCOOMe	5-thiazolyl
S	n-pentyl	OCOOMe	2-pyrimidinyl
S	n-pentyl	OCOOMe	4-pyrimidinyl
S	n-pentyl	OCOOMe	5-pyrimidinyl
S	n-pentyl	OCOOMe	2-indolyl
S	n-pentyl	OCOOMe	3-indolyl
S	n-pentyl	OCOOMe	5-indolyl
S	n-pentyl	OCOOMe	6-indolyl
S	n-pentyl	OCOOMe	5-benzimidazolyl
S	n-pentyl	OCOOMe	2-benzofuryl
S	n-pentyl	OCOOMe	3-indazolyl
S	n-pentyl	OCOOMe	2-benzoxazolyl
S	n-pentyl	OCOOMe	4-fluoro-1-naphthyl
S	n-pentyl	OCOOMe	5-chloro-2-thienyl
S	n-pentyl	OCOOMe	4-methyl-1-naphthyl
S	n-pentyl	OCOOMe	1-methyl-2-pyrrolyl
S	n-pentyl	OCOOMe	2-methyl-3-furyl
S	n-pentyl	OCOOMe	5-methyl-2-thienyl
S	n-pentyl	OCOOMe	4-methyl-5-imidazolyl
S	n-pentyl	OCOOMe	1-methyl-3-indolyl
S	n-pentyl	OCOOMe	2-methoxy-1-naphthyl
S	n-pentyl	OCOOMe	3-methoxy-2-naphthyl
S	n-pentyl	OCOOMe	6-ethoxy-2-naphthyl
S	n-pentyl	OCOOMe	5-methoxy-3-indolyl
S	n-pentyl	OCOOMe	1,4-dimethoxy-2-naphthyl
S	n-pentyl	OCOOMe	5,6-dimethoxy-2-indolyl
S	n-pentyl	OCOOMe	5-methoxy-1-methyl-2-indolyl
S	n-pentyl	OCOOEt	1-naphthyl
S	n-pentyl	OCOOEt	2-naphthyl
S	n-pentyl	OCOOEt	2-pyrrolyl
S	n-pentyl	OCOOEt	3-pyrrolyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-pentyl	OCOOEt	2-furyl
S	n-pentyl	OCOOEt	3-furyl
S	n-pentyl	OCOOEt	2-thienyl
S	n-pentyl	OCOOEt	3-thienyl
S	n-pentyl	OCOOEt	3-pyrazolyl
S	n-pentyl	OCOOEt	4-pyrazolyl
S	n-pentyl	OCOOEt	2-imidazolyl
S	n-pentyl	OCOOEt	4-imidazolyl
S	n-pentyl	OCOOEt	2-oxazolyl
S	n-pentyl	OCOOEt	4-oxazolyl
S	n-pentyl	OCOOEt	5-oxazolyl
S	n-pentyl	OCOOEt	2-thiazolyl
S	n-pentyl	OCOOEt	4-thiazolyl
S	n-pentyl	OCOOEt	5-thiazolyl
S	n-pentyl	OCOOEt	2-pyrimidinyl
S	n-pentyl	OCOOEt	4-pyrimidinyl
S	n-pentyl	OCOOEt	5-pyrimidinyl
S	n-pentyl	OCOOEt	2-indolyl
S	n-pentyl	OCOOEt	3-indolyl
S	n-pentyl	OCOOEt	5-indolyl
S	n-pentyl	OCOOEt	6-indolyl
S	n-pentyl	OCOOEt	5-benzimidazolyl
S	n-pentyl	OCOOEt	2-benzofuryl
S	n-pentyl	OCOOEt	3-indazolyl
S	n-pentyl	OCOOEt	2-benzoxazolyl
S	n-pentyl	OCOOEt	4-fluoro-1-naphthyl
S	n-pentyl	OCOOEt	5-chloro-2-thienyl
S	n-pentyl	OCOOEt	4-methyl-1-naphthyl
S	n-pentyl	OCOOEt	1-methyl-2-pyrrolyl
S	n-pentyl	OCOOEt	2-methyl-3-furyl
S	n-pentyl	OCOOEt	5-methyl-2-thienyl
S	n-pentyl	OCOOEt	4-methyl-5-imidazolyl
S	n-pentyl	OCOOEt	1-methyl-3-indolyl
S	n-pentyl	OCOOEt	2-methoxy-1-naphthyl
S	n-pentyl	OCOOEt	3-methoxy-2-naphthyl
S	n-pentyl	OCOOEt	6-ethoxy-2-naphthyl
S	n-pentyl	OCOOEt	5-methoxy-3-indolyl
S	n-pentyl	OCOOEt	1,4-dimethoxy-2-naphthyl

Table 1 (continued)

X	R^1	R^2	Y
S	n-pentyl	OCOOEt	5,6-dimethoxy-2-indolyl
S	n-pentyl	OCOOEt	5-methoxy-1-methyl-2-indolyl
NH	2-methoxyethyl	OH	1-naphthyl
NH	2-methoxyethyl	OH	2-naphthyl
NH	2-methoxyethyl	OH	2-pyrrolyl
NH	2-methoxyethyl	OH	3-pyrrolyl
NH	2-methoxyethyl	OH	2-furyl
NH	2-methoxyethyl	OH	3-furyl
NH	2-methoxyethyl	OH	2-thienyl
NH	2-methoxyethyl	OH	3-thienyl
NH	2-methoxyethyl	OH	3-pyrazolyl
NH	2-methoxyethyl	OH	4-pyrazolyl
NH	2-methoxyethyl	OH	2-imidazolyl
NH	2-methoxyethyl	OH	4-imidazolyl
NH	2-methoxyethyl	OH	2-oxazolyl
NH	2-methoxyethyl	OH	4-oxazolyl
NH	2-methoxyethyl	OH	5-oxazolyl
NH	2-methoxyethyl	OH	2-thiazolyl
NH	2-methoxyethyl	OH	4-thiazolyl
NH	2-methoxyethyl	OH	5-thiazolyl
NH	2-methoxyethyl	OH	2-pyrimidinyl
NH	2-methoxyethyl	OH	4-pyrimidinyl
NH	2-methoxyethyl	OH	5-pyrimidinyl
NH	2-methoxyethyl	OH	2-indolyl
NH	2-methoxyethyl	OH	3-indolyl
NH	2-methoxyethyl	OH	5-indolyl
NH	2-methoxyethyl	OH	6-indolyl
NH	2-methoxyethyl	OH	5-benzimidazolyl
NH	2-methoxyethyl	OH	2-benzofuryl
NH	2-methoxyethyl	OH	3-indazolyl
NH	2-methoxyethyl	OH	2-benzoxazolyl
NH	2-methoxyethyl	OH	4-fluoro-1-naphthyl
NH	2-methoxyethyl	OH	5-chloro-2-thienyl
NH	2-methoxyethyl	OH	4-methyl-1-naphthyl
NH	2-methoxyethyl	OH	1-methyl-2-pyrrolyl
NH	2-methoxyethyl	OH	2-methyl-3-furyl
NH	2-methoxyethyl	OH	5-methyl-2-thienyl
NH	2-methoxyethyl	OH	4-methyl-5-imidazolyl

Table 1 (continued)

X	R^1	R^2	Y
NH	2-methoxyethyl	OH	1-methyl-3-indolyl
NH	2-methoxyethyl	OH	2-methoxy-1-naphthyl
NH	2-methoxyethyl	OH	3-methoxy-2-naphthyl
NH	2-methoxyethyl	OH	6-ethoxy-2-naphthyl
NH	2-methoxyethyl	OH	5-methoxy-3-indolyl
NH	2-methoxyethyl	OH	1,4-dimethoxy-2-naphthyl
NH	2-methoxyethyl	OH	5,6-dimethoxy-2-indolyl
NH	2-methoxyethyl	OH	5-methoxy-1-methyl-2-indolyl
NH	3-methoxypropyl	OH	1-naphthyl
NH	3-methoxypropyl	OH	2-naphthyl
NH	3-methoxypropyl	OH	2-pyrrolyl
NH	3-methoxypropyl	OH	3-pyrrolyl
NH	3-methoxypropyl	OH	2-furyl
NH	3-methoxypropyl	OH	3-furyl
NH	3-methoxypropyl	OH	2-thienyl
NH	3-methoxypropyl	OH	3-thienyl
NH	3-methoxypropyl	OH	3-pyrazolyl
NH	3-methoxypropyl	OH	4-pyrazolyl
NH	3-methoxypropyl	OH	2-imidazolyl
NH	3-methoxypropyl	OH	4-imidazolyl
NH	3-methoxypropyl	OH	2-oxazolyl
NH	3-methoxypropyl	OH	4-oxazolyl
NH	3-methoxypropyl	OH	5-oxazolyl
NH	3-methoxypropyl	OH	2-thiazolyl
NH	3-methoxypropyl	OH	4-thiazolyl
NH	3-methoxypropyl	OH	5-thiazolyl
NH	3-methoxypropyl	OH	2-pyrimidinyl
NH	3-methoxypropyl	OH	4-pyrimidinyl
NH	3-methoxypropyl	OH	5-pyrimidinyl
NH	3-methoxypropyl	OH	2-indolyl
NH	3-methoxypropyl	OH	3-indolyl
NH	3-methoxypropyl	OH	5-indolyl
NH	3-methoxypropyl	OH	6-indolyl
NH	3-methoxypropyl	OH	5-benzimidazolyl
NH	3-methoxypropyl	OH	2-benzofuryl
NH	3-methoxypropyl	OH	3-indazolyl
NH	3-methoxypropyl	OH	2-benzoxazolyl
NH	3-methoxypropyl	OH	4-fluoro-1-naphthyl

Table 1 (continued)

X	R^1	R^2	Y
NH	3-methoxypropyl	OH	5-chloro-2-thienyl
NH	3-methoxypropyl	OH	4-methyl-1-naphthyl
NH	3-methoxypropyl	OH	1-methyl-2-pyrrolyl
NH	3-methoxypropyl	OH	2-methyl-3-furyl
NH	3-methoxypropyl	OH	5-methyl-2-thienyl
NH	3-methoxypropyl	OH	4-methyl-5-imidazolyl
NH	3-methoxypropyl	OH	1-methyl-3-indolyl
NH	3-methoxypropyl	OH	2-methoxy-1-naphthyl
NH	3-methoxypropyl	OH	3-methoxy-2-naphthyl
NH	3-methoxypropyl	OH	6-ethoxy-2-naphthyl
NH	3-methoxypropyl	OH	5-methoxy-3-indolyl
NH	3-methoxypropyl	OH	1,4-dimethoxy-2-naphthyl
NH	3-methoxypropyl	OH	5,6-dimethoxy-2-indolyl
NH	3-methoxypropyl	OH	5-methoxy-1-methyl-2-indolyl
O	2-methoxyethyl	OH	1-naphthyl
O	2-methoxyethyl	OH	2-naphthyl
O	2-methoxyethyl	OH	2-pyrrolyl
O	2-methoxyethyl	OH	3-pyrrolyl
O	2-methoxyethyl	OH	2-furyl
O	2-methoxyethyl	OH	3-furyl
O	2-methoxyethyl	OH	2-thienyl
O	2-methoxyethyl	OH	3-thienyl
O	2-methoxyethyl	OH	3-pyrazolyl
O	2-methoxyethyl	OH	4-pyrazolyl
O	2-methoxyethyl	OH	2-imidazolyl
O	2-methoxyethyl	OH	4-imidazolyl
O	2-methoxyethyl	OH	2-oxazolyl
O	2-methoxyethyl	OH	4-oxazolyl
O	2-methoxyethyl	OH	5-oxazolyl
O	2-methoxyethyl	OH	2-thiazolyl
O	2-methoxyethyl	OH	4-thiazolyl
O	2-methoxyethyl	OH	5-thiazolyl
O	2-methoxyethyl	OH	2-pyrimidinyl
O	2-methoxyethyl	OH	4-pyrimidinyl
O	2-methoxyethyl	OH	5-pyrimidinyl
O	2-methoxyethyl	OH	2-indolyl
O	2-methoxyethyl	OH	3-indolyl
O	2-methoxyethyl	OH	5-indolyl

Table 1 (continued)

X	R^1	R^2	Y
O	2-methoxyethyl	OH	6-indolyl
O	2-methoxyethyl	OH	5-benzimidazolyl
O	2-methoxyethyl	OH	2-benzofuryl
O	2-methoxyethyl	OH	3-indazolyl
O	2-methoxyethyl	OH	2-benzoxazolyl
O	2-methoxyethyl	OH	4-fluoro-1-naphthyl
O	2-methoxyethyl	OH	5-chloro-2-thienyl
O	2-methoxyethyl	OH	4-methyl-1-naphthyl
O	2-methoxyethyl	OH	1-methyl-2-pyrrolyl
O	2-methoxyethyl	OH	2-methyl-3-furyl
O	2-methoxyethyl	OH	5-methyl-2-thienyl
O	2-methoxyethyl	OH	4-methyl-5-imidazolyl
O	2-methoxyethyl	OH	1-methyl-3-indolyl
O	2-methoxyethyl	OH	2-methoxy-1-naphthyl
O	2-methoxyethyl	OH	3-methoxy-2-naphthyl
O	2-methoxyethyl	OH	6-ethoxy-2-naphthyl
O	2-methoxyethyl	OH	5-methoxy-3-indolyl
O	2-methoxyethyl	OH	1,4-dimethoxy-2-naphthyl
O	2-methoxyethyl	OH	5,6-dimethoxy-2-indolyl
O	2-methoxyethyl	OH	5-methoxy-1-methyl-2-indolyl
O	3-methoxypropyl	OH	1-naphthyl
O	3-methoxypropyl	OH	2-naphthyl
O	3-methoxypropyl	OH	2-pyrrolyl
O	3-methoxypropyl	OH	3-pyrrolyl
O	3-methoxypropyl	OH	2-furyl
O	3-methoxypropyl	OH	3-furyl
O	3-methoxypropyl	OH	2-thienyl
O	3-methoxypropyl	OH	3-thienyl
O	3-methoxypropyl	OH	3-pyrazolyl
O	3-methoxypropyl	OH	4-pyrazolyl
O	3-methoxypropyl	OH	2-imidazolyl
O	3-methoxypropyl	OH	4-imidazolyl
O	3-methoxypropyl	OH	2-oxazolyl
O	3-methoxypropyl	OH	4-oxazolyl
O	3-methoxypropyl	OH	5-oxazolyl
O	3-methoxypropyl	OH	2-thiazolyl
O	3-methoxypropyl	OH	4-thiazolyl
O	3-methoxypropyl	OH	5-thiazolyl

Table 1 (continued)

X	R^1	R^2	Y
O	3-methoxypropyl	OH	2-pyrimidinyl
O	3-methoxypropyl	OH	4-pyrimidinyl
O	3-methoxypropyl	OH	5-pyrimidinyl
O	3-methoxypropyl	OH	2-indolyl
O	3-methoxypropyl	OH	3-indolyl
O	3-methoxypropyl	OH	5-indolyl
O	3-methoxypropyl	OH	6-indolyl
O	3-methoxypropyl	OH	5-benzimidazolyl
O	3-methoxypropyl	OH	2-benzofuryl
O	3-methoxypropyl	OH	3-indazolyl
O	3-methoxypropyl	OH	2-benzoxazolyl
O	3-methoxypropyl	OH	4-fluoro-1-naphthyl
O	3-methoxypropyl	OH	5-chloro-2-thienyl
O	3-methoxypropyl	OH	4-methyl-1-naphthyl
O	3-methoxypropyl	OH	1-methyl-2-pyrrolyl
O	3-methoxypropyl	OH	2-methyl-3-furyl
O	3-methoxypropyl	OH	5-methyl-2-thienyl
O	3-methoxypropyl	OH	4-methyl-5-imidazolyl
O	3-methoxypropyl	OH	1-methyl-3-indolyl
O	3-methoxypropyl	OH	2-methoxy-1-naphthyl
0	3-methoxypropyl	OH	3-methoxy-2-naphthyl
O	3-methoxypropyl	OH	6-ethoxy-2-naphthyl
O	3-methoxypropyl	OH	5-methoxy-3-indolyl
O	3-methoxypropyl	OH	1,4-dimethoxy-2-naphthyl
O	3-methoxypropyl	OH	5,6-dimethoxy-2-indolyl
O	3-methoxypropyl	OH	5-methoxy-1-methyl-2-indolyl
S	2-methoxyethyl	OH	1-naphthyl
S	2-methoxyethyl	OH	2-naphthyl
S	2-methoxyethyl	OH	2-pyrrolyl
S	2-methoxyethyl	OH	3-pyrrolyl
S	2-methoxyethyl	OH	2-furyl
S	2-methoxyethyl	OH	3-furyl
S	2-methoxyethyl	OH	2-thienyl
S	2-methoxyethyl	OH	3-thienyl
S	2-methoxyethyl	OH	3-pyrazolyl
S	2-methoxyethyl	OH	4-pyrazolyl
S	2-methoxyethyl	OH	2-imidazolyl
S	2-methoxyethyl	OH	4-imidazolyl

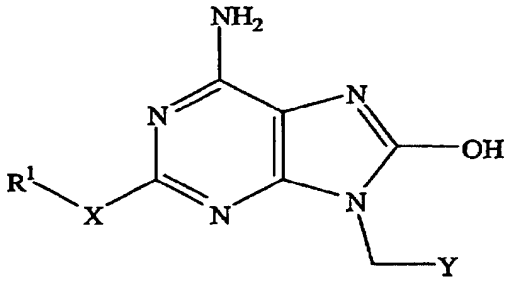
Table 1 (continued)

X	R^1	R^2	Y
S	2-methoxyethyl	OH	2-oxazolyl
S	2-methoxyethyl	OH	4-oxazolyl
S	2-methoxyethyl	OH	5-oxazolyl
S	2-methoxyethyl	OH	2-thiazolyl
S	2-methoxyethyl	OH	4-thiazolyl
S	2-methoxyethyl	OH	5-thiazolyl
S	2-methoxyethyl	OH	2-pyrimidinyl
S	2-methoxyethyl	OH	4-pyrimidinyl
S	2-methoxyethyl	OH	5-pyrimidinyl
S	2-methoxyethyl	OH	2-indolyl
S	2-methoxyethyl	OH	3-indolyl
S	2-methoxyethyl	OH	5-indolyl
S	2-methoxyethyl	OH	6-indolyl
S	2-methoxyethyl	OH	5-benzimidazolyl
S	2-methoxyethyl	OH	2-benzofuryl
S	2-methoxyethyl	OH	3-indazolyl
S	2-methoxyethyl	OH	2-benzoxazolyl
S	2-methoxyethyl	OH	4-fluoro-1-naphthyl
S	2-methoxyethyl	OH	5-chloro-2-thienyl
S	2-methoxyethyl	OH	4-methyl-1-naphthyl
S	2-methoxyethyl	OH	1-methyl-2-pyrrolyl
S	2-methoxyethyl	OH	2-methyl-3-furyl
S	2-methoxyethyl	OH	5-methyl-2-thienyl
S	2-methoxyethyl	OH	4-methyl-5-imidazolyl
S	2-methoxyethyl	OH	1-methyl-3-indolyl
S	2-methoxyethyl	OH	2-methoxy-1-naphthyl
S	2-methoxyethyl	OH	3-methoxy-2-naphthyl
S	2-methoxyethyl	OH	6-ethoxy-2-naphthyl
S	2-methoxyethyl	OH	5-methoxy-3-indolyl
S	2-methoxyethyl	OH	1,4-dimethoxy-2-naphthyl
S	2-methoxyethyl	OH	5,6-dimethoxy-2-indolyl
S	2-methoxyethyl	OH	5-methoxy-1-methyl-2-indolyl
S	2-hydroxyethyl	OH	1-naphthyl
S	2-hydroxyethyl	OH	2-naphthyl
S	2-hydroxyethyl	OH	2-pyrrolyl
S	2-hydroxyethyl	OH	3-pyrrolyl
S	2-hydroxyethyl	OH	2-furyl
S	2-hydroxyethyl	OH	3-furyl

Table 1 (continued)

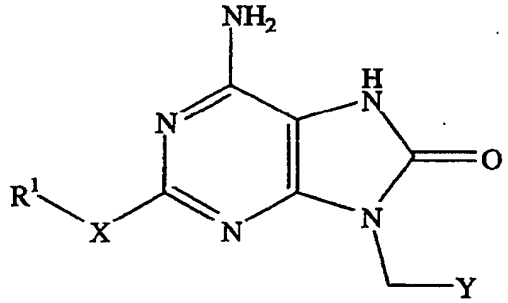
X	R^1	R^2	Y
S	2-hydroxyethyl	OH	2-thienyl
S	2-hydroxyethyl	OH	3-thienyl
S	2-hydroxyethyl	OH	3-pyrazolyl
S	2-hydroxyethyl	OH	4-pyrazolyl
S	2-hydroxyethyl	OH	2-imidazolyl
S	2-hydroxyethyl	OH	4-imidazolyl
S	2-hydroxyethyl	OH	2-oxazolyl
S	2-hydroxyethyl	OH	4-oxazolyl
S	2-hydroxyethyl	OH	5-oxazolyl
S	2-hydroxyethyl	OH	2-thiazolyl
S	2-hydroxyethyl	OH	4-thiazolyl
S	2-hydroxyethyl	OH	5-thiazolyl
S	2-hydroxyethyl	OH	2-pyrimidinyl
S	2-hydroxyethyl	OH	4-pyrimidinyl
S	2-hydroxyethyl	OH	5-pyrimidinyl
S	2-hydroxyethyl	OH	2-indolyl
S	2-hydroxyethyl	OH	3-indolyl
S	2-hydroxyethyl	OH	5-indolyl
S	2-hydroxyethyl	OH	6-indolyl
S	2-hydroxyethyl	OH	5-benzimidazolyl
S	2-hydroxyethyl	OH	2-benzofuryl
S	2-hydroxyethyl	OH	3-indazolyl
S	2-hydroxyethyl	OH	2-benzoxazolyl
S	2-hydroxyethyl	OH	4-fluoro-1-naphthyl
S	2-hydroxyethyl	OH	5-chloro-2-thienyl
S	2-hydroxyethyl	OH	4-methyl-1-naphthyl
S	2-hydroxyethyl	OH	1-methyl-2-pyrrolyl
S	2-hydroxyethyl	OH	2-methyl-3-furyl
S	2-hydroxyethyl	OH	5-methyl-2-thienyl
S	2-hydroxyethyl	OH	4-methyl-5-imidazolyl
S	2-hydroxyethyl	OH	1-methyl-3-indolyl
S	2-hydroxyethyl	OH	2-methoxy-1-naphthyl
S	2-hydroxyethyl	OH	3-methoxy-2-naphthyl
S	2-hydroxyethyl	OH	6-ethoxy-2-naphthyl
S	2-hydroxyethyl	OH	5-methoxy-3-indolyl
S	2-hydroxyethyl	OH	1,4-dimethoxy-2-naphthyl
S	2-hydroxyethyl	OH	5,6-dimethoxy-2-indolyl
S	2-hydroxyethyl	OH	5-methoxy-1-methyl-2-indolyl

[0032] A compound in which R^2 represents acyloxy or alkoxycarbonyloxy according to the present invention is equivalent to ester of a compound in which R^2 represents hydroxyl. The compound is a prodrug that is aimed at improving solubility, absorbency, and biostability of a compound in which R^2 represents hydroxyl. That is, the above ester is metabolized in a living organism to an active form compound in which R^2 is hydroxyl. A compound represented by general formula (I) and a tautomer thereof are chemically equivalent. The adenine derivative according to the present invention includes the tautomer. For example, when R^2 represent hydroxyl, a compound represented by general formula (I) is a hydroxy derivative represented by general formula (II):



(II)

wherein R^1, X, and Y are as defined in general formula (I). An example of a tautomer of this derivative is an oxo derivative represented by general formula (III):



(III)

wherein R', X, and Y are as defined in general formula (I).

[0033] An embodiment of a process for producing these adenine derivatives is hereafter described in detail.

(1) When R^2 is OH

[0034] A compound (IV) is allowed to react with Y-CH_2-Hal (wherein Y is as defined in general formula (II) and Hal represents a halogen atom) in the presence of a base, thereby synthesizing a 9-substitution product (V). Examples of the aforementioned bases that can be used include alkali metal salt or alkaline earth metal salt of carbonic acid such as potassium carbonate, metal hydroxides such as sodium hydroxide and potassium hydroxide, metal hydrides such as sodium hydride, and alkoxides such as potassum t-butoxide. Examples of the aforementioned solvents that can be used include aprotic solvents such as dimethylformamide, dimethyl sulfoxide, tetrahydrofuran, and 1,4-dioxane. Reaction temperature can be between room temperature and reflux temperature of the solvent.

[0035] Subsequently, when X represents NH, a compound (V) is allowed to react with a corresponding R^1-NH_2 (wherein R^1 is as defined above) in the presence or absence of a base, thereby synthesizing a 2-substitution product (VI). Examples of bases that can be used include tertiary amines such as triethylamine, diisopropylethylamine, and 4-dimethylaminopyridine. Examples of solvents that can be used include aprotic solvents, such as tetrahydrofuran, 1,4-dioxane, and diglyme, and alcoholic solvents such as propanol or butanol. Alternatively, reaction may be carried out in the absence of a solvent. Reaction temperature can be between 50°C and reflux temperature of the solvent.

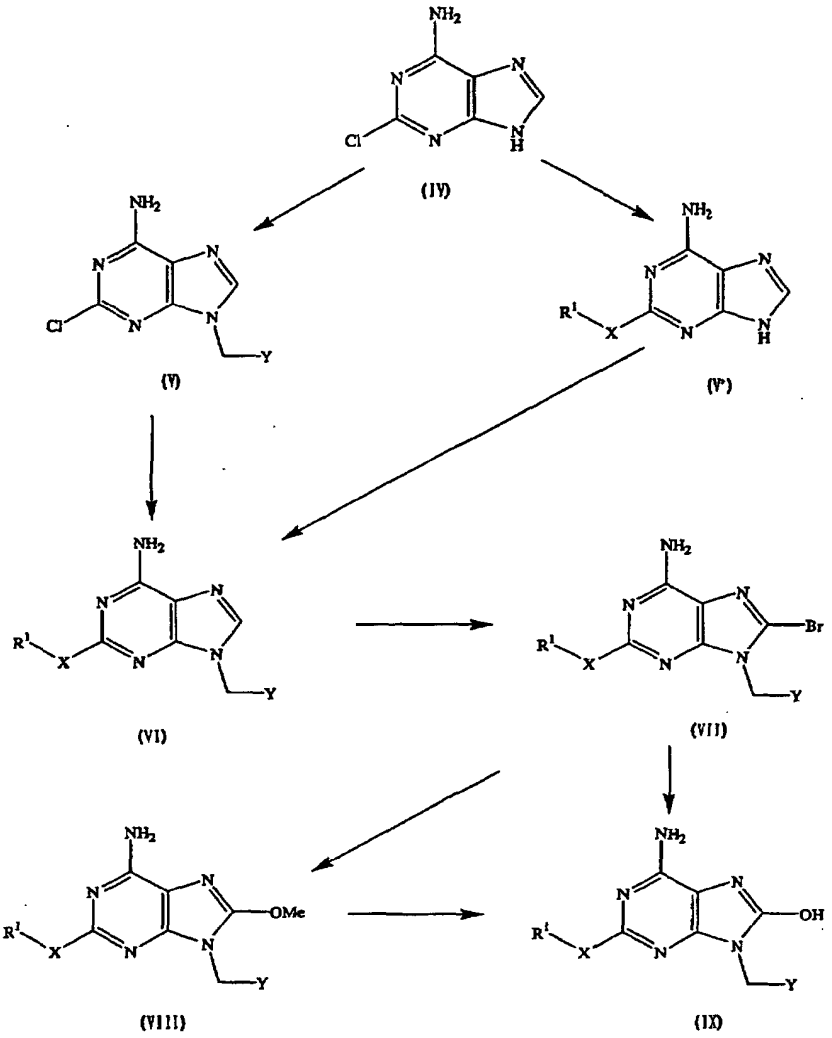
[0036] When X represents an oxygen atom or sulfur atom, a compound (V) is allowed to react with a corresponding R^1-OH or R^1-SH in the presence of a base, thereby synthesizing a 2-substitution product (VI). Examples of bases that

can be used include alkali metals such as sodium or potassium and alkali metal hydrides such as sodium hydride. Examples of solvents that can be used include aprotic solvents such as dimethylformamide, dimethyl sulfoxide, tetrahydrofuran, 1,4-dioxane, and diglyme. Alternatively, reaction may be carried out in the absence of a solvent. Reaction temperature can be between 50°C and reflux temperature of the solvent.

[0037] In a process for producing a compound (VI) from a compound (IV), a compound (VI) can be obtained by first synthesizing a 2-substitution product (V'), followed by the reaction between the 2-substitution product (V') and Y-CH_2-Hal (wherein Y is as defined in general formula (II) and Hal represents a halogen atom).

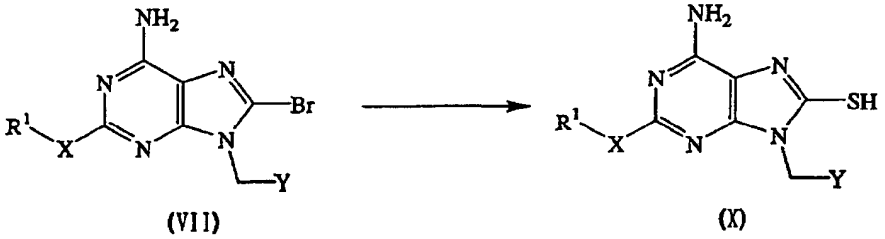
[0038] A compound (VII) can be synthesized by reacting a compound (VI) with bromine. Examples of solvents that can be used include, halogenated solvents such as carbon tetrachloride, dichloromethane or chloroform, and acetic acid. Reaction temperature can be between 0°C and reflux temperature of the solvent. Alternatively, a reaction assistant such as sodium acetate may be additionally used in the reaction.

[0039] A compound (IX) can be synthesized through hydrolysis of a compound (VII) under acidic conditions. Examples of acids that can be used include hydrochloric acid and hydrobromic acid. Reaction temperature can be between 50°C and reflux temperature of the solvent. Alternatively, a compound (VII) is allowed to react with sodium methoxide to prepare a compound (VIII), and the resultant is treated with acid for demethylation. Thus, a compound (IX) can be obtained.



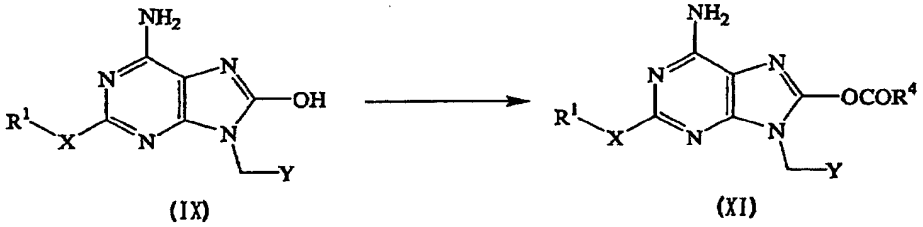
[0040] A compound (X) can be synthesized by reacting a compound (VII) with sodium hydrosulfide (sodium hydrogensulfide). Examples of solvents that can be used include alcoholic solvents such as ethanol, propanol, and butanol.

Reaction temperature can be between 50°C and reflux temperature of the solvent.



(VII) (X)

[0041] A compound (XI) can be obtained by allowing the compound (IX) to react with acyl chloride or chloroformate ester corresponding to R^2 in the presence of a base. Examples of bases that can be used include tertiary amines such as triethylamine, diisopropylethylamine, or 4-dimethylaminopyridine. Examples of solvents that can be used include aprotic solvents such as tetrahydrofuran, 1,4-dioxane, and dichloromethane. Reaction temperature can be between 0°C and reflux temperature of the solvent (In the formula, R^4 represents C_{1-7} alkyl or C_{1-7} alkoxy).



(IX) (XI)

[0042] The thus obtained adenine derivative according to the present invention can be used as a pharmaceutically acceptable salt such as sodium salt, potassium salt, calcium salt, hydrochloride, hydrobromate, sulfate, nitrate, acetate, methanesulfonate, toluenesulfonate, citrate, fumarate, or maleate.

[0043] The adenine derivative according to the present invention is useful as a therapeutic agent for viral diseases such as hepatitis B, hepatitis C, and AIDS, cancerous diseases, and diseases resulting from type 2 helper T cells. It can be used in various dosage forms, for example, oral preparations such as a tablet, capsule, or powder. In addition, it can be parenteral injection or external preparation. The pharmaceutical preparation according to the present invention can be any substance selected from the group consisting of a compound represented by general formula (I), a tautomer thereof, and a pharmaceutically acceptable salt thereof. A hydrate or solvate thereof may also be used. Alternatively, two or more of these substances may be used in combinations. A substance itself that is selected from the aforementioned group may be administered as a pharmaceutical preparation according to the present invention. In general, however, it is preferably administered in a form of a pharmaceutical composition comprising, as an active ingredient, the aforementioned substance and a pharmaceutically acceptable additive for pharmaceutical preparations.

[0044] A pharmaceutical composition for organisms can be easily produced in accordance with a process that is common in the field of pharmaceutical preparations, wherein the aforementioned substance as an active ingredient is mixed with at least one pharmaceutically acceptable additive for pharmaceutical preparations. A route for administering the pharmaceutical preparation according to the present invention is not particularly limited. Preferably, the most effective route is suitably selected for therapy and/or prevention. Examples of pharmaceutical compositions that are suitable for oral administration include capsules, powders, tablets, granules, fine grains, syrups, liquids, and suspensions. Examples of pharmaceutical compositions that are suitable for parenteral administration include inhalants, sprays, intrarectal preparations, parenteral injections, drops, pastes, creams, percutaneous absorbents, transmucosal absorbents, eye drops, nasal drops, ear drops, tapes, and medical applications. It should be noted that the forms of the pharmaceutical preparation according to the present invention are not limited thereto.

[0045] Among the pharmaceutical compositions suitable for oral administration, for example, liquid preparations such as emulsions and syrups can be produced using additives for pharmaceutical preparations. Examples thereof include: water; saccharine such as sucrose, sorbit, and fructose; glycols such as polyethylene glycol and propylene glycol; oils such as sesame oil, olive oil, and soybean oil; antiseptics such as p-hydroxybenzoate; and flavors such as strawberry flavor and peppermint. Solid preparations such as capsules, tablets, powders, and granules can be produced using:

for example, excipients such as lactose, glucose, sucrose, and mannite; disintegrators such as starch and sodium alginate; lubricants such as magnesium stearate and talc; binders such as polyvinyl alcohol, hydroxypropylcellulose, and gelatin; surfactants such as fatty acid ester; and plasticizers such as glycerin.

[0046] Among pharmaceutical compositions suitable for parenteral administration, liquid preparations such as parenteral injections, drops, and eye drops can be preferably produced as sterilized isotonic liquid preparations. For example, parenteral injections can be produced using an aqueous medium comprising a mixture of a salt solution, a glucose solution, or salt water and a glucose solution. Intrarectal preparations can be generally produced in a form of suppository using, for example, a carrier such as cacao butter, hydrogenated fat, or hydrogenated carboxylic acid. Sprays can be prepared using nonirritating carriers that allow the aforementioned substances as active ingredients to be dispersed as fine particles to facilitate absorption. Examples of such carriers include lactose and glycerin. A form of aerosol or dry powder preparation can be selected. Also, at least one additive for pharmaceutical preparations selected from diluent, flavor, antiseptics, excipient, disintegrator, lubricant, binder, surfactant, plasticizer, and the like as exemplified in the production of oral preparation can be suitably used to produce a pharmaceutical composition for parenteral administration. It should be noted that additives for pharmaceutical preparations that are used to produce the pharmaceutical preparation according to the present invention are not limited to the aforementioned substances. Any substance can be used as long as it is available to persons skilled in the art.

[0047] The dose of the adenine derivative according to the present invention is suitably determined depending on, for example, sex, age, body weight, type of disease, or symptom of a patient. The dose is generally in the range of 0.001 to 100 mg/kg per day, and preferably in the range of 0.01 to 10 mg/kg. Administration can be made in single or several separate doses.

[0048] This description includes part or all of the content as disclosed in the description of Japanese Patent Application No. 2001-118232, which is a priority document of the present application.

Brief Description of Drawings

[0049]

Fig. 1 is a diagram showing the result of evaluation for the medicinal effect of the compound according to the present invention in a rat model of eosinophil leukocytic infiltration.

Fig. 2 is a diagram showing the result of evaluation for the medicinal effect of the compound according to the present invention in a mouse model of active cutaneous anaphylaxis.

Fig. 3 is a diagram showing the result of evaluation for the antitumor effect described in Example 65, wherein the tumor volume of the compound of Example 27 and that of mouse interferon α were compared with that of the vehicle (a control group).

Fig. 4 is a diagram showing the result of evaluation for the antitumor effect described in Example 66 (the effect of inhibiting metastasis), wherein the wet weight of each lymph node was compared among the group to which the vehicle was administered (the control group), the group to which mouse interferon α was administered, and the group to which the compound of Example 27 was administered.

Best Modes for Carrying out the Invention

[0050] The present invention is hereafter described in detail with reference to the examples, although the technical scope of the present invention is not limited thereto.

Reference Example 1: 2-Butoxyadenine

[0051] Sodium (13.6 g, 0.59 mol) was added to butanol (480 ml), the temperature of the mixture was raised to 90°C to completely dissolve sodium therein. Subsequently, 2-chloroadenine (4.0 g, 23.6 mmol) was added, and the resultant was heated under reflux for 9 hours. After the reaction solution was cooled to 4°C, water (400 ml) was added thereto, and the resultant was vigorously stirred for 30 minutes. The separated layer of butanol was concentrated under reduced pressure, water (400 ml) was added to the residue, and concentrated hydrochloric acid was added dropwide under ice cooling to neutralize the product. The precipitated solid was collected by filtration, the resulting solid was added to ethanol (70 ml), and the resultant was heated under reflux for 30 minutes. The product was cooled to room temperature, and the precipitated solid was then collected by filtration. Thus, 3.72 g of the title compound was obtained (yield: 76%).

Reference Example 2: 8-Bromo-2-butoxy-9-(6-chloro-3-pyridylmethyl)adenine

[0052] Potassium carbonate (2.85 g, 20.6 mmol) and 2-chloro-5-chloromethylpyridine (3.33 g, 20.6 mmol) were add-

ed to the DMF solution (125 ml) of 2-butoxyadenine (2.60 g, 12.5 mmol) obtained in Reference Example 1. The resultant was stirred while heating at 80°C for 2.5 hours. The reaction solution was concentrated under reduced pressure, water (100 ml) was added thereto, and the resultant was neutralized with 1N hydrochloric acid. The precipitated solid was collected by filtration. The resulting solid was dissolved in methylene chloride (100 ml), hexane (150 ml) was added under ice cooling, and the precipitated crystal was collected by filtration. Thus, 2-butoxy-9-(6-chloro-3-pyridylmethyl) adenine was obtained (yield: 3.12 g). Bromine (1.92 ml, 37.5 mmol) was added to an acetic acid suspension (186 ml) comprising sodium acetate (3.05 g, 37.2 mmol) and 2-butoxy-9-(6-chloro-3-pyridylmethyl)adenine (3.1 g, 9.31 mmol) at room temperature, and the resultant was allowed to react for 4 hours. The reaction solution was removed by distillation under reduced pressure, water (200 ml) was added to the residue, and the resultant was neutralized with 5N sodium hydroxide under ice cooling. The precipitated crystal was collected by filtration, and crude crystal was recrystalized with the aid of methanol. The resultant was dried under reduced pressure at 40°C for 15 hours. Thus, 2.38 g of the title compound was obtained as a white powdery crystal (yield: 62%).

Reference Example 3: 2-Butoxy-9-(6-chloro-3-pyridylmethyl)-8-methoxyadenine

[0053] Sodium (614 mg, 26.7 mmol) was added and completely dissolved in methanol (110 ml). 8-Bromo-2-butoxy-9-(6-chloro-3-pyridylmethyl)adenine (2.2 g, 5.34 mmol) obtained in Reference Example 2 was added to the resulting solution, and the mixture was heated under reflux for 3.5 hours. The reaction solution was concentrated under reduced pressure, water (100 ml) was added to the residue, and the resultant was neutralized with concentrated hydrochloric acid under ice cooling. The precipitated solid was collected by filtration and washed with water (20 ml). This solid was recrystalized with the aid of ethyl acetate (30 ml) to obtain 1.26 g of the title compound as a white powdery crystal (yield: 65.0%).

Reference Example 4: 2-Butoxy-9-(6-methoxy-3-pyridylmethyl)adenine

[0054] Sodium (415 mg, 18.0 mmol) was added and completely dissolved in methanol (18 ml). Thereafter, 2-butoxy-9-(6-chloro-3-pyridylmethyl)adenine (300 mg, 0.90 mmol) was added thereto, and the resultant was heated under reflux for 24 hours. The reaction solution was concentrated under reduced pressure, water (30 ml) was added to the residue, and the resultant was neutralized with concentrated hydrochloric acid under ice cooling. The precipitated solid was collected by filtration, and crude crystal was purified by silica gel column chromatography (methylene chloride:methanol = 50:1) to obtain 148 mg of the title compound (yield: 50%).

Reference Example 5: 2-Butylaminoadenine

[0055] 2-Chloroadenine (6.0 g, 35.4 mmol) and butylamine (30 ml) were placed in an autoclave (200 ml), and the content of the autoclave was allowed to react at 130°C for 150 hours. The reaction solution was concentrated under reduced pressure, and water was poured into the residue to precipitate a solid. The precipitated solid was sequentially washed with methylene chloride and methanol. Thus, 2.08 g of the title compound was obtained as a yellowish orange powdery solid (yield: 30%).

Example 1: 2-Butoxy-9-(6-chloro-3-pyridylmethyl)-8-hydroxyadenine

[0056] The compound (1.26 g, 3.47 mmol) obtained in Reference Example 3 was added to concentrated hydrochloric acid (70 ml), and the mixture was allowed to react at room temperature for 2 hours. The reaction solution was concentrated under reduced pressure, water (130 ml) was added to the residue, and the resultant was neutralized with an aqueous solution of 5N sodium hydroxide under ice cooling. The precipitated crystal was collected by filtration and then dried. Thus, 1.20 g of the title compound was obtained as a white powdery crystal (yield: 99%).
^{1}H NMR (DMSO-d_6) δ 10.14 (1H, brs), 8.40 (1H, d, J = 2.4 Hz), 7.76 (1H, dd, J = 2.4, 8.4 Hz), 7.49 (1H, d, J = 8.4 Hz), 6.55 (2H, brs), 4.91 (2H, s), 4.14 (2H, t, J = 6.5 Hz), 1.67-1.57 (2H, m), 1.44-1.30 (2H, m), 0.90 (3H, t, J = 7.3 Hz).

Example 2: 2-Butoxy-8-hydroxy-9-(6-methoxy-3-pyridylmethyl)adenine

[0057] The title compound was obtained in the same manner as in Example 1 using a corresponding starting material.
^{1}H NMR (DMSO-d_6) δ 10.09 (1H, brs), 8.16 (1H, d, J = 2.4 Hz), 7.65 (1H, dd, J = 2.4, 8.4 Hz), 6.78 (1H, d, J = 8.4 Hz), 6.49 (2H, brs), 4.80 (2H, s), 4.15 (2H, t, J = 6.6 Hz), 3.81 (3H, s), 1.66-1.58 (2H, m), 1.42-1.34 (2H, m), 0.91 (3H, t, J = 7.3 Hz).

Example 3: 2-Butoxy-9-(6-ethoxy-3-pyridylmethyl)-8-hydroxyadenine

[0058] The title compound was obtained in the same manner as in Example 1 using a corresponding starting material. ^{1}H NMR (DMSO-d_6) δ 10.06 (1H, brs), 8.14 (1H, d, J = 2.4 Hz), 7.64 (1H, dd, J = 2.4, 8.6 Hz), 6.75 (1H, d, J = 8.6 Hz), 6.48 (2H, brs), 4.80 (2H, s), 4.26 (2H, q, J = 7.2 Hz), 4.15 (2H, t, J = 6.6 Hz), 1.68-1.58 (2H, m), 1.42-1.34 (2H, m), 1.28 (3H, t, J = 7.2 Hz), 0.91 (3H, t, J = 7.3 Hz).

Example 4: 2-Butoxy-9-(6-n-butoxy-3-pyridylmethyl)-8-hydroxyadenine

[0059] The title compound was obtained in the same manner as in Example 1 using a corresponding starting material. ^{1}H NMR (DMSO-d_6) δ 10.25 (1H, brs), 8.13 (1H, d, J = 1.9 Hz), 7.63 (1H, dd, J = 1.9, 8.4 Hz), 6.75 (1H, d, J = 8.4 Hz), 6.53 (2H, brs), 4.79 (2H, s), 4.23-4.12 (4H, m), 1.68-1.60 (4H, m), 1.42-1.34 (4H, m), 0.94-0.88 (6H, m).

Example 5: 2-Butoxy-9-(2-chloro-3-pyridylmethyl)-8-hydroxyadenine

[0060] The title compound was obtained in the same manner as in Example 1 using a corresponding starting material. ^{1}H NMR (DMSO-d_6) δ 10.15 (1H, brs), 8.36-8.33 (1H, m), 7.52-7.50 (1H, m), 7.41-7.36 (1H, m), 6.53 (2H, brs), 4.94 (2H, s), 4.07 (2H, t, J = 6.6 Hz), 1.62-1.52 (2H, m), 1.37-1.23 (2H, m), 0.87 (3H, t, J = 7.3 Hz).

Example 6: 2-Butoxy-8-hydroxy-9-(2-methoxy-3-pyridylmethyl)adenine

[0061] The title compound was obtained in the same manner as in Example 1 using a corresponding starting material. ^{1}H NMR (DMSO-d_6) δ 10.06 (1H, brs), 8.08-8.06 (1H, m), 7.21-7.19 (1H, m), 6.93-6.88 (1H, m), 6.47 (2H, brs), 4.80 (2H, s), 4.08 (2H, t, J = 6.5 Hz), 3.92 (3H, s), 1.60-1.53 (2H, m), 1.38-1.29 (2H, m), 0.87 (3H, t, J = 7.3 Hz).

Example 7: 2-Butoxy-9-(6-chloro-5-methoxy-3-pyridylmethyl)-8-hydroxyadenine

[0062] The title compound was obtained in the same manner as in Example 1 using a corresponding starting material. ^{1}H NMR (DMSO-d_6) δ 10.06 (1H, brs), 8.12 (1H, d, J = 1.9 Hz), 7.85 (1H, d, J = 1.9 Hz), 6.49 (2H, brs), 4.83 (2H, s), 4.16 (2H, t, J = 6.6 Hz), 3.91 (3H, s), 1.66-1.61 (2H, m), 1.42-1.34 (2H, m), 0.91 (3H, t, J = 7.3 Hz).

Example 8: 2-Butoxy-8-hydroxy-9-(3-pyridylmethyl)adenine

[0063] Potassium carbonate (1.1 g, 8 mmol) and 3-chloromethylpyridine hydrochloride (660 mg, 5 mmol) were added to a DMF solution (30 ml) comprising 2-chloroadenine (520 mg, 3 mmol), and the resultant was stirred while heating at 80°C for 3 hours. The reaction solution was concentrated under reduced pressure, water was added thereto, and the precipitated solid was collected by filtration. Thus, 2-chloro-9-(3-pyridylmethyl)adenine was obtained (yield: 759 mg). Sodium (750 mg, 30 mmol) was added to butanol (50 ml), and the temperature of the mixture was raised to 90°C to completely dissolve sodium therein. Subsequently, 2-chloro-9-(3-pyridylmethyl)adenine (430 mg, 1.5 mmol) was added thereto, and the resultant was heated under reflux for 2 hours. The solvent was concentrated under reduced pressure, water was added to the residue, and concentrated hydrochloric acid was added dropwise under ice cooling to neutralize the solution. Liquid separation was carried out with the addition of methylene chloride, and the organic layer was concentrated under reduced pressure. Acetic acid (30 ml) was added to the residue to dissolve it, bromine (660 mg, 5.5 mmol) was added thereto, and the resultant was allowed to react at room temperature all day and night. The reaction solution was removed by distillation under reduced pressure, and the residue was purified by silica gel column chromatography (methylene chloride:methanol = 10:1). Thus, 310 mg of 8-bromo-2-butoxy-9-(3-pyridylmethyl) adenine was obtained. Subsequently, the title compound was obtained in the same manner as in Reference Example 3 and Example 1.
^{1}H NMR (DMSO-d_6) δ 10.22 (1H, brs), 8.56 (1H, d, J = 1.9 Hz), 8.49-8.47 (1H, m), 7.71-7.67 (1H, m), 7.38-7.33 (1H, m), 6.54 (2H, brs), 4.90 (2H, s), 4.14 (2H, t, J = 6.6 Hz), 1.65-1.57 (2H, m), 1.41-1.33 (2H, m), 0.90 (3H, t, J = 7.3 Hz).

Example 9: 2-Butoxy-8-hydroxy-9-(4-pyridylmethyl)adenine

[0064] The title compound was obtained in the same manner as in Example 1 using a corresponding starting material. ^{1}H NMR (DMSO-d_6) δ 10.20 (1H, brs), 8.70-8.68 (2H, m), 7.29-7.27 (2H, m), 6.48 (2H, brs), 4.92 (2H, s), 4.16 (2H, t, J = 6.6 Hz), 1.63-1.55 (2H, m), 1.40-1.32 (2H, m), 0.89 (3H, t, J = 7.3 Hz).

Example 10: 2-Butoxy-9-(pyrazin-2-ylmethyl)-8-methoxyadenine

[0065] The title compound was obtained in the same manner as in Example 1 using a corresponding starting material.
^{1}H NMR (DMSO-d_6) δ 10.02 (1H, brs), 8.66 (1H, s), 8.56-8.53 (2H, m), 6.48 (2H, brs), 5.05 (2H, s), 4.06 (2H, t, J = 6.6 Hz), 1.59-1.51 (2H, m), 1.37-1.29 (2H, m), 0.87 (3H, t, J = 7.3 Hz).

Example 11: 2-Butoxy-9-(5,6-dichloro-3-pyridylmethyl)-8-hydroxyadenine

[0066] Concentrated hydrochloric acid (4 ml) was added to a butanol suspension (4 ml) comprising 2-n-butoxy-8-bromo-9-(5,6-dichloro-3-pyridylmethyl)-8-hydroxyadenine (150 mg, 0.34 mmol) obtained in the same manner as in Reference Example 2, and the resultant was allowed to react at 70°C for 9 hours. The reaction solution was concentrated under reduced pressure, water (30 ml) was added to the residue under ice cooling, and the solution was neutralized with an aqueous solution of 1N sodium hydroxide. The precipitated solid was collected by filtration, crude crystal was purified by silica gel column chromatography (methylene chloride:methanol = 25:1), and 45 mg of the title compound was obtained as a white powdery crystal (yield: 35%).
^{1}H NMR (DMSO-d_6) δ 10.16 (1H, brs), 8.36 (1H, d, J = 1.9 Hz), 8.06 (1H, d, J = 1.9 Hz), 6.52 (2H, brs), 4.93 (2H, s), 4.13 (2H, t, J = 6.6 Hz), 1.64-1.58 (2H, m), 1.40-1.32 (2H, m), 0.90 (3H, t, J = 7.3 Hz).

Example 12: 2-Butoxy-9-(2,6-dichloro-3-pyridylmethyl)-8-hydroxyadenine

[0067] The title compound was obtained in the same manner as in Example 11 using a corresponding starting material.
^{1}H NMR (DMSO-d_6) δ 10.12 (1H, brs), 7.66 (1H, d, J = 8.4 Hz), 7.52 (1H, d, J = 8.4 Hz), 6.52 (2H, brs), 4.92 (2H, s), 4.08 (2H, t, J = 6.6 Hz), 1.60-1.52 (2H, m), 1.37-1.29 (2H, m), 0.88 (3H, t, J = 7.4 Hz).

Example 13: 2-Butoxy-9-(6-piperidino-3-pyridylmethyl)-8-hydroxyadenine

[0068] The compound (100 mg, 0.29 mmol) obtained in Example 1 was added to piperidine (3 ml), and the resultant was allowed to react at 90°C for 30 hours. The reaction solution was concentrated under reduced pressure, and methylene chloride (50 ml) was added to the residue to precipitate a solid. The precipitated solid was collected by filtration and washed with water. Thus, 56 mg of the title compound was obtained as a white powdery solid (yield: 49%).
^{1}H NMR (DMSO-d_6) δ 9.79 (1H, brs), 8.09 (1H, d, J = 2.4 Hz), 7.47 (1H, dd, J = 2.4, 8.6 Hz), 6.75 (1H, d, J = 8.6 Hz), 6.44 (2H, brs), 4.70 (2H, s), 4.17 (2H, t, J = 6.5 Hz), 3.48-3.44 (4H, m), 1.67-1.35 (10H, m), 0.92 (3H, t, J = 7.3 Hz).

Example 14: 2-Butoxy-9-(6-(1-pyrrolidinyl)-3-pyridylmethyl)-8-hydroxyadenine

[0069] The title compound was obtained in the same manner as in Example 13 using the compound obtained in Example 1 and pyrrolidine.
^{1}H NMR (DMSO-d_6) δ 10.03 (1H, brs), 8.07 (1H, d, J = 2.4 Hz), 7.46 (1H, dd, J = 2.4, 8.6 Hz), 6.45 (2H, brs), 6.37 (1H, d, J = 8.6 Hz), 4.69 (2H, s), 4.16 (2H, t, J = 6.6 Hz), 3.33-3.29 (4H, m), 1.93-1.88 (4H, m), 1.67-1.59 (2H, m), 1.43-1.35 (2H, m), 0.92 (3H, t, J = 7.3 Hz).

Example 15: 2-Butoxy-9-(6-morpholino-3-pyridylmethyl)-8-hydroxyadenine

[0070] The title compound was obtained in the same manner as in Example 13 using the compound obtained in Example 1 and morpholine.
^{1}H NMR (DMSO-d_6) δ 10.01 (1H, brs), 8.14 (1H, d, J = 2.4 Hz), 7.53 (1H, dd, J = 2.4, 8.6 Hz), 6.78 (1H, d, J = 8.6 Hz), 6.45 (2H, brs), 4.73 (2H, s), 4.16 (2H, t, J = 6.6 Hz), 3.66 (4H, t, J = 4.9 Hz), 3.38 (4H, t, J = 4.9 Hz), 1.67-1.61 (2H, m), 1.43-1.35 (2H, m), 0.92 (3H, t, J = 7.3 Hz).

Example 16: 2-Butoxy-9-(6-dimethylamino-3-pyridylmethyl)-8-hydroxyadenine

[0071] The title compound was obtained in the same manner as in Example 13 using the compound obtained in Example 1 and an aqueous solution of 40% dimethylamine.
^{1}H NMR (DMSO-d_6) δ 10.12 (1H, brs), 8.09 (1H, d, J = 2.4 Hz), 7.48 (1H, dd, J = 2.4, 8.9 Hz), 6.57 (1H, d, J = 8.9 Hz), 6.49 (2H, brs), 4.70 (2H, s), 4.16 (2H, t, J = 6.6 Hz), 2.97 (6H, s), 1.70-1.46 (2H, m), 1.43-1.33 (2H, m), 0.92 (3H, t, J = 7.3 Hz).

Example 17: 2-Butylamino-9-(6-chloro-3-pyridylmethyl)-8-hydroxyadenine

[0072] The title compound was obtained in the same manner as in Example 11 using the compound obtained in Reference Example 5.
^{1}H NMR (DMSO-d_6) δ 10.10 (1H, brs), 8.56 (1H, d, J = 1.9 Hz), 8.49-8.47 (1H, m), 7.71-7.67 (1H, m), 7.38-7.33 (1H, m), 6.50 (2H, brs), 4.90 (2H, s), 4.14 (2H, t, J = 6.6 Hz), 1.67-1.57 (2H, m), 1.41-1.30 (2H, m), 0.90 (3H, t, J = 7.3 Hz).

Example 18: 2-Butylamino-9-(2-chloro-3-pyridylmethyl)-8-hydroxyadenine

[0073] The title compound was obtained in the same manner as in Example 11 using the compound obtained in Reference Example 5.
^{1}H NMR (DMSO-d_6) δ 9.76 (1H, brs), 8.35-8.32 (1H, m), 7.47-7.36 (2H, m), 6.23 (1H, brt, J = 5.7 Hz), 6.07 (2H, s), 4.88 (2H, s), 3.13-3.05 (2H, m), 1.43-1.27 (2H, m), 1.24-1.16 (2H, m), 0.82 (3H, t, J = 7.3 Hz).

Example 19: 2-Butylamino-8-hydroxy-9-(6-methoxy-3-pyridylmethyl)adenine

[0074] The title compound was obtained in the same manner as in Example 11 using the compound obtained in Reference Example 5.
^{1}H NMR (DMSO-d_6) δ 10.07 (1H, brs), 8.17 (1H, d, J = 2.4 Hz), 7.67 (1H, dd, J = 2.4, 8.4 Hz), 6.82-6.76 (2H, m), 6.60 (2H, brs), 4.78 (2H, s), 3.81 (3H, s), 3.25-3.17 (2H, m), 1.54-1.43 (2H, m), 1.38-1.25 (2H, m), 0.89 (3H, t, J = 7.3 Hz).

Example 20: 2-Butylamino-8-hydroxy-9-(2-pyridylmethyl)adenine

[0075] The title compound was obtained in the same manner as in Example 11 using the compound obtained in Reference Example 5.
^{1}H NMR (DMSO-d_6) δ 10.88 (1H, s), 8.56-8.54 (1H, m), 8.05-7.89 (3H, m), 7.46-7.41 (2H, m), 5.05 (3H, s), 3.19-3.14 (2H, m), 1.44-1.21 (4H, m), 0.81 (3H, t, J = 7.3 Hz).

Example 21: 2-Butylamino-8-hydroxy-9-(3-pyridylmethyl)adenine

[0076] The title compound was obtained in the same manner as in Example 11 using the compound obtained in Reference Example 5.
^{1}H NMR (DMSO-d_6) δ 9.78 (1H, brs), 8.55 (1H, d, J = 2.4 Hz), 8.47 (1H, dd, J = 1.9, 4.9 Hz), 7.68 (1H, d, J = 7.8 Hz), 7.34 (1H, dd, J = 4.9, 7.8 Hz), 6.21 (1H, brt, J = 5.5 Hz), 6.05 (2H, brs), 4.84 (2H, s), 3.20-3.12 (2H, m), 1.47-1.39 (2H, m), 1.32-1.24 (2H, m), 0.87 (3H, t, J = 7.3 Hz).

Example 22: 2-Butylamino-8-hydroxy-9-(4-pyridylmethyl)adenine

[0077] The title compound was obtained in the same manner as in Example 11 using the compound obtained in Reference Example 5.
^{1}H NMR (DMSO-d_6) δ 11.05 (1H, brs), 8.76 (2H, d, J = 8.7 Hz), 8.09-7.88 (3H, m), 7.73 (2H, d, J = 8.7 Hz), 5.09 (2H, s), 3.22-3.17 (2H, m), 1.47-1.32 (2H, m), 1.29-1.18 (2H, m), 0.82 (3H, t, J = 7.4 Hz).

Example 23: 2-Butylamino-9-(2,6-dichloro-3-pyridylmethyl)-8-hydroxyadenine

[0078] The title compound was obtained in the same manner as in Example 11 using the compound obtained in Reference Example 5.
^{1}H NMR (DMSO-d_6) δ 9.82 (1H, brs), 7.61-7.51 (2H, m), 6.23 (1H, brt, J = 5.4 Hz), 6.08 (2H, s), 4.87 (2H, s), 3.12-3.05 (2H, m), 1.40-1.19 (4H, m), 0.82 (3H, t, J = 7.3 Hz).

Example 24: 2-Butylamino-9-(6-dimethylamino-3-pyridylmethyl)-8-hydroxyadenine

[0079] The title compound was obtained in the same manner as in Example 13 using the compound obtained in Example 17 and an aqueous solution of 40% dimethylamine.
^{1}H NMR (DMSO-d_6) δ 9.61 (1H, brs), 8.10 (1H, d, J = 2.2 Hz), 7.49 (1H, dd, J = 2.2, 8.6 Hz), 6.56 (1H, d, J = 8.6 Hz), 6.18 (1H, brt, J = 5.7 Hz), 5.97 (2H, brs), 4.65 (2H, s), 3.22-3.15 (2H, m), 2.97 (6H, s), 1.53-1.42 (2H, m), 1.38-1.24 (2H, m), 0.89 (3H, t, J = 7.3 Hz).

Example 25: 2-Butoxy-8-hydroxy-9-(6-methyl-3-pyridylmethyl)adenine

[0080] The title compound was obtained in the same manner as in Example 1 using a corresponding starting material.
^{1}H NMR (DMSO-d_6) δ 9.95 (1H, s), 8.42 (1H, d, J = 2.2 Hz), 7.58 (1H, dd, J = 2.2, 8.1 Hz), 7.20 (1H, d, J = 8.1 Hz), 6.46 (2H, brs), 4.84 (2H, s), 4.14 (2H, t, J = 6.6 Hz), 2.41 (3H, s), 1.62 (2H, m), 1.37 (2H, m), 0.90 (3H, t, J = 7.3 Hz).

Example 26: 2-Butoxy-8-hydroxy-9-(2-methyl-3-pyridylmethyl)adenine

[0081] The title compound was obtained in the same manner as in Example 1 using a corresponding starting material.
^{1}H NMR (DMSO-d_6) δ 10.01 (1H, brs), 8.33 (1H, d, J = 3.1 Hz), 7.39 (1H, d, J = 6.4 Hz), 7.15 (1H, dd, J = 3.1, 6.4 Hz), 6.49 (2H, brs), 4.88 (2H, s), 4.10 (2H, t, J = 6.6 Hz), 2.59 (3H, s), 1.59 (2H, m), 1.34 (2H, m), 0.88 (3H, t, J = 7.3 Hz).

Example 27: 2-Butylamino-8-hydroxy-9-(6-methyl-3-pyridylmethyl)adenine

[0082] The title compound was obtained in the same manner as in Example 11 using the compound obtained in Reference Example 5.
^{1}H NMR (DMSO-d_6) δ 9.78 (1H, s), 8.42 (1H, d, J = 2.2 Hz), 7.57 (1H, dd, J = 2.2, 8.0 Hz), 7.19 (1H, d, J = 8.0 Hz), 6.22 (1H, t, J = 7.1 Hz), 6.09 (2H, brs), 4.78 (2H, s), 3.16 (2H, m), 2.41 (3H, s), 1.44 (2H, m), 1.28 (2H, m), 0.87 (3H, t, J = 9.6 Hz).

Example 28: 2-Butylamino-8-hydroxy-9-(2-methyl-3-pyridylmethyl)adenine

[0083] The title compound was obtained in the same manner as in Example 11 using the compound obtained in Reference Example 5.
^{1}H NMR (DMSO-d_6) δ 9.70 (1H, s), 8.32 (1H, d, J = 3.1 Hz), 7.37 (1H, d, J = 7.7 Hz), 7.14 (1H, dd, J = 3.1, 7.7 Hz), 6.20 (1H, t, J = 6.4 Hz), 6.0 (2H, brs), 4.82 (2H, s), 3.12 (2H, m), 2.60 (3H, s), 1.39 (2H, m), 1.25 (2H, m), 0.84 (3H, t, J = 7.1 Hz).

Example 29: 2-Butylamino-9-(2-chloro-6-methyl-3-pyridylmethyl)-8-hydroxyadenine

[0084] The title compound was obtained in the same manner as in Example 11 using the compound obtained in Reference Example 5.
^{1}H NMR (DMSO-d_6) δ 9.74 (1H, brs), 7.33 (1H, d, J = 5.8 Hz), 7.22 (1H, d, J = 5.8 Hz), 6.24 (1H, m), 6.06 (2H, brs), 4.83 (2H, s), 3.09 (2H, m), 2.42 (3H, s), 1.37 (2H, m), 1.25 (2H, m), 0.82 (3H, t, J = 5.5 Hz).

Example 30: 2-Butylamino-8-hydroxy-9-(6-hydroxy-3-pyridylmethyl)adenine

[0085] The title compound was obtained in the same manner as in Example 11 using the compound obtained in Reference Example 5.
^{1}H NMR (DMSO-d_6) δ 11.50 (1H, brs), 9.61 (1H, brs), 7.45 (1H, dd, J = 2.6, 9.5 Hz), 7.28 (1H, d, J = 2.6 Hz), 6.28 (1H, d, J = 9.5 Hz), 6.22 (1H, t, J = 6. 2 Hz), 6.00 (2H, brs), 4.53 (2H, s), 3.17 (2H, q, J =6.2 Hz), 1.45 (2H, m), 1.30 (2H, m), 0.88 (3H, t, J = 7.3 Hz).

Example 31: 8-Hydroxy-2-(2-methoxy)ethoxy-9-(3-pyridylmethyl)adenine

[0086] The title compound was obtained in the same manner as in Example 1 using a corresponding starting material.
^{1}H NMR (DMSO-d_6) δ 10.02 (1H, brs), 8.57 (1H, s), 8.48 (1H, d, J = 4.8 Hz), 7.70 (1H, d, J = 6.1 Hz), 7.36 (1H, dd, J = 4.8, 6.1 Hz), 6.50 (2H, brs), 4.90 (2H, s), 4.27 (2H, t, J = 4.6 Hz), 3.59 (2H, t, J = 4.6 Hz), 3.27 (3H, s).

Example 32: 8-Hydroxy-2-methoxy-9-(3-pyridylmethyl)adenine

[0087] The title compound was obtained in the same manner as in Example 1.
^{1}H NMR (DMSO-d_6) δ 10.04 (1H, brs), 8.57 (1H, s), 8.48 (1H, d, J = 4.8 Hz), 7.71 (1H, d, J = 6.1 Hz), 7.35 (1H, dd, J = 4.8, 6.1 Hz), 6.53 (2H, brs), 4.90 (2H, s), 3.76 (3H, s).

Example 33: 2-Butylamino-8-ethoxycarbonyloxy-9-(6-methoxy-3-pyridylmethyl)adenine

[0088] Triethylamine (100 μL, 0.75 mmol), ethyl chloroformate (67 μL, 0.70 mmol), and dimethylaminopyridine (20

mg, 0.17 mmol) were added to a solution (15 ml) of the compound (200 mg, 0.58 mmol) obtained in Example 19 in methylene chloride in that order, and the resultant was allowed to react at room temperature for 15 hours. Water was added to the reaction solution to extract an organic layer. The organic layer was washed with an aqueous solution of 5% citric acid and 10% saline solution and dried over anhydrous sodium sulfate. The solvent was then removed by distillation. Hexane was added to the residue, and the solid was precipitated, followed by collection by filtration. Thus, 170 mg of the title compound was obtained as a white powdery solid (yield: 71%).
^{1}H NMR ($CDCl_3$) δ 8.33 (1H, d, J = 1.9 Hz), 7.75 (1H, dd, J = 1.9, 8.4 Hz), 6.15 (2H, brs), 6.67 (1H, d, J = 8.4 Hz), 4.87 (2H, s), 4.71 (1H, brt, J = 5.4 Hz), 4.46 (2H, q, J = 7.1 Hz), 3.90 (3H, s), 3.41-3.34 (2H, m), 1.60-1.35 (7H, m), 0.96 (3H, t, J = 7.3 Hz).

Example 34: 2-Butylamino-9-(6-chloro-3-pyridylmethyl)-8-ethoxycarbonyloxyadenine

[0089] The title compound was obtained in the same manner as in Example 33 using the compound obtained in Example 17 and ethyl chloroformate.
^{1}H NMR ($CDCl_3$) δ 8.55 (1H, d, J = 2.4 Hz), 7.81 (1H, dd, J = 2.4, 8.4 Hz), 7.27 (1H, d, J = 8.4 Hz), 6.06 (2H, brs), 4.93 (2H, s), 4.83 (1H, brt, J = 5.5 Hz), 4.47 (2H, q, J = 7.1 Hz), 3.40-3.32 (2H, m), 1.59-1.36 (7H, m), 0.95 (3H, t, J = 7.3 Hz).

Example 35: 2-Butylamino-8-isopropoxycarbonyloxy-9-(6-methoxy-3-pyridylmethyl)adenine

[0090] The title compound was obtained in the same manner as in Example 33 using the compound obtained in Example 19 and isopropyl chloroformate.
^{1}H NMR ($CDCl_3$) δ 8.32 (1H, d, J = 2.2 Hz), 7.74 (1H, dd, J = 2.2, 8.9 Hz), 6.68 (1H, d, J = 8.9 Hz), 6.08 (2H, brs), 5.23-5.13 (1H, m), 4.89 (1H, brt, J = 5.8 Hz), 4.87 (2H, s), 3.91 (3H, s), 3.42-3.35 (2H, m), 1.60-1.52 (2H, m), 1.48-1.37 (8H, m), 0.96 (3H, t, J = 7.3 Hz).

Example 36: 2-Butylamino-9-(6-chloro-3-pyridylmethyl)-8-isopropoxycarbonyloxyadenine

[0091] The title compound was obtained in the same manner as in Example 33 using the compound obtained in Example 17 and isopropyl chloroformate.
^{1}H NMR ($CDCl_3$) δ 8.55 (1H, d, J = 1.9 Hz), 7.80 (1H, dd, J = 1.9, 8.4 Hz), 7.27 (1H, d, J = 8.4 Hz), 6.14 (2H, brs), 5.24-5.14 (1H, m), 4.96-4.92 (3H, m), 3.40-3.33 (2H, m), 1.62-1.51 (2H, m), 1.45-1.34 (8H, m), 0.95 (3H, t, J = 7.3 Hz).

Example 37: 2-Butoxy-8-ethoxycarbonyloxy-9-(6-methoxy-3-pyridylmethyl)adenine

[0092] The title compound was obtained in the same manner as in Example 33 using the compound obtained in Example 2 and ethyl chloroformate.
^{1}H NMR ($CDCl_3$) δ 8.33 (1H, d, J = 2.4 Hz), 7.75 (1H, dd, J = 2.4, 8.1 Hz), 6.68 (1H, d, J = 8.1 Hz), 6.15 (2H, brs), 4.93 (2H, s), 4.48 (2H, q, J = 7.1 Hz), 4.30 (2H, t, J = 6.6 Hz), 3.90 (3H, s), 1.83-1.72 (2H, m), 1.53-1.43 (5H, m), 0.98 (3H, t, J = 7.3 Hz).

Example 38: 2-Butoxy-9-(6-chloro-3-pyridylmethyl)-8-ethoxycarbonyloxyadenine

[0093] The title compound was obtained in the same manner as in Example 33 using the compound obtained in Example 1 and ethyl chloroformate.
^{1}H NMR ($CDCl_3$) δ 8.56 (1H, d, J = 2.4 Hz), 7.81 (1H, dd, J = 2.4, 8.4 Hz), 7.29 (1H, d, J = 8.4 Hz), 7.28 (2H, brs), 4.99 (2H, s), 4.49 (2H, q, J = 7.0 Hz), 4.28 (2H, t, J = 6.6 Hz), 1.81-1.71 (2H, m), 1.52-1.43 (5H, m), 0.97 (3H, t, J = 7.3 Hz).

Example 39: 2-Butoxy-9-(2-chloro-3-pyridylmethyl)-8-ethoxycarbonyloxyadenine

[0094] The title compound was obtained in the same manner as in Example 33 using the compound obtained in Example 5 and ethyl chloroformate.
^{1}H NMR (DMSO-d_6) δ 8.37-8.35 (1H, m), 7.73-7.69 (1H, m), 7.41-7.37 (1H, m), 7.09 (2H, brs), 4.95 (2H, s), 4.39 (2H, q, J = 7.2 Hz), 4.12 (2H, t, J = 6.6 Hz), 1.61-1.53 (2H, m), 1.37-1.29 (5H, m), 0.87 (3H, t, J = 7.3 Hz).

Example 40: 2-Butoxy-8-methoxycarbonyloxy-9-(3-pyridylmethyl)adenine

[0095] The title compound was obtained in the same manner as in Example 33 using the compound obtained in Example 8 and methyl chloroformate.

^{1}H NMR ($CDCl_3$) δ 8.77 (1H, d, J = 2.2 Hz), 8.56-8.53 (1H, m), 7.85-7.81 (1H, m), 7.25 (2H, brs), 7.24-7.22 (1H, m), 5.02 (2H, s), 4.30 (2H, t, J = 6.6 Hz), 4.05 (3H, s), 1.82-1.72 (2H, m), 1.53-1.42 (2H, m), 0.97 (3H, t, J = 7.3 Hz).

Example 41: 2-Butoxy-8-(n-pentyloxy)carbonyloxy-9-(3-pyridylmethyl)adenine

[0096] The title compound was obtained in the same manner as in Example 33 using the compound obtained in Example 8 and n-pentyl chloroformate.
^{1}H NMR (DMSO-d_6) δ 8.59 (1H, d, J = 1.9 Hz), 8.51-8.48 (1H, m), 7.75-7.72 (1H, m), 7.39-7.34 (1H, m), 7.07 (2H, brs), 4.92 (2H, s), 4.32 (2H, t, J = 6.6 Hz), 4.18 (2H, t, J = 6.5 Hz), 1.71-1.61 (4H, m), 1.41-1.31 (6H, m), 0.93-0.85 (6H, m).

Example 42: 2-Butoxy-8-(cyclohexyloxy)carbonyloxy-9-(3-pyridylmethyl)adenine

[0097] The title compound was obtained in the same manner as in Example 33 using the compound obtained in Example 8 and cyclohexyl chloroformate.
^{1}H NMR (DMSO-d_6) δ 8.60 (1H, d, J = 1.9 Hz), 8.51-8.49 (1H, m), 7.76-7.72 (1H, m), 7.39-7.35 (1H, m), 7.07 (2H, brs), 4.96-4.93 (3H, m), 4.18 (2H, t, J = 6.5 Hz), 1.86-1.58 (8H, m), 1.44-1.33 (6H, m), 0.91 (3H, t, J = 7.4 Hz).

Example 43: 8-(Allyloxy)carbonyloxy-2-butoxy-9-(3-pyridylmethyl)adenine

[0098] The title compound was obtained in the same manner as in Example 33 using the compound obtained in Example 8 and allyl chloroformate.
^{1}H NMR (DMSO-d_6) δ 8.61 (1H, d, J = 1.9 Hz), 8.51-8.49 (1H, m), 7.77-7.74 (1H, m), 7.39-7.35 (1H, m), 7.25 (1H, dd, J = 6.5, 13.8 Hz), 7.03 (2H, brs), 5.06 (1H, dd, J = 1.9, 13.8 Hz), 4.93 (2H, s), 4.86 (1H, dd, J = 1.9, 6.5 Hz), 4.19 (2H, t, J = 6.6 Hz), 1.64-1.41 (2H, m), 1.39-1.33 (2H, m), 0.91 (3H, t, J = 7.4 Hz).

Example 44: 8-Acetyloxy-2-butoxy-9-(6-chloro-3-pyridylmethyl)adenine

[0099] The title compound was obtained in the same manner as in Example 33 using the compound obtained in Example 17 and acetic anhydride.
^{1}H NMR ($CDCl_3$) δ 8.56 (1H, d, J = 2.4 Hz), 7.80 (1H, dd, J = 2.4, 8.4 Hz), 7.30 (1H, d, J = 8.4 Hz), 7.28 (2H, brs), 5.00 (2H, s), 4.29 (2H, t, J = 6.5 Hz), 2.72 (3H, s), 1.82-1.71 (2H, m), 1.52-1.42 (2H, m), 0.97 (3H, t, J = 7.3 Hz).

Example 45: 8-Propionyloxy-2-butoxy-9-(6-chloro-3-pyridylmethyl)adenine

[0100] The title compound was obtained in the same manner as in Example 33 using the compound obtained in Example 17 and propionyl chloride.
^{1}H NMR ($CDCl_3$) δ 8.55 (1H, d, J = 2.4 Hz), 7.80 (1H, dd, J = 2.4, 8.1 Hz), 7.30 (1H, d, J = 8.1 Hz), 7.28 (2H, brs), 5.00 (2H, s), 4.29 (2H, t, J = 6.5 Hz), 3.14 (2H, q, J = 7.4 Hz), 1.82-1.71 (2H, m), 1.55-1.42 (2H, m), 1.23 (3H, t, J = 7.3 Hz), 0.97 (3H, t, J = 7.3 Hz).

Example 46: 8-Benzoyloxy-2-butoxy-9-(6-methyl-3-pyridylmethyl)adenine

[0101] The title compound was obtained in the same manner as in Example 33 using the compound obtained in Example 25 and benzoyl chloride.
^{1}H NMR ($CDCl_3$) δ 8.64 (1H, d, J = 2.4 Hz), 7.77 (2H, d, J = 7.3 Hz), 7.69 (1H, dd, J = 2.4, 8.1 Hz), 7.63 (1H, t, J = 7.3 Hz), 7.49 (2H, t, J = 7.3 Hz), 7.09 (1H, d, J = 8.1 Hz), 5.76 (2H, brs), 4.95 (2H, s), 4.34 (2H, t, J = 6.6 Hz), 2.52 (3H, s), 1.78 (2H, m), 1.52 (2H, m), 0.99 (3H, t, J = 7.3 Hz).

Example 47: 8-Benzoyloxy-2-butylamino-9-(6-methyl-3-pyridylmethyl)adenine

[0102] The title compound was obtained in the same manner as in Example 33 using the compound obtained in Example 27 and benzoyl chloride.
^{1}H NMR ($CDCl_3$) δ 8.63 (1H, d, J = 2.0 Hz), 7.74 (2H, d, J = 7.4 Hz), 7.69 (1H, dd, J = 2.0, 7.9 Hz), 7.61 (1H, t, J = 7.4 Hz), 7.47 (2H, t, J = 7.4 Hz), 7.08 (1H, d, J = 7.9 Hz), 5.57 (2H, brs), 4.88 (2H, s), 4.84 (1H, t, J = 5.9 Hz), 3.40 (2H, m), 2.52 (3H, s), 1.58 (2H, m), 1.42 (2H, m), 0.97 (3H, t, J = 7.3 Hz).

Example 48: 2-Butoxy-8-(4-methyl)benzoyloxy-9-(6-methyl-3-pyridylmethyl)adenine

[0103] The title compound was obtained in the same manner as in Example 33 using the compound obtained in Example 25 and p-toluoyl chloride.
^{1}H NMR (DMSO-d_6) δ 8.44 (1H, s), 7.73 (2H, d, J = 8.2 Hz), 7.62 (1H, d, J = 8.0 Hz), 7.30 (2H, d, J = 8.2 Hz), 7.20 (1H, d, J = 8.0 Hz), 6.84 (2H, brs), 4.84 (2H, s), 4.22 (2H, t, J = 6.6 Hz), 2.42 (3H, s), 2.40(3H, s), 1.66 (2H, m), 1.41 (2H, m), 0.92 (3H, t, J = 7.4 Hz).

Example 49: 2-Butylamino-8-(4-methyl)benzoyloxy-9-(6-methyl-3-pyridylmethyl)adenine

[0104] The title compound was obtained in the same manner as in Example 33 using the compound obtained in Example 27 and p-toluoyl chloride.
^{1}H NMR (DMSO-d_6) δ 8.43 (1H, s), 7.69 (2H, d, J = 8.2 Hz), 7.62 (1H, d, J = 8.0 Hz), 7.28 (2H, d, J = 8.2 Hz), 7.19 (1H, d, J = 8.0 Hz), 6.71 (1H, brs), 6.25 (2H, brs), 4.80 (2H, s), 3.22 (2H, t, J = 6.6 Hz), 2.42 (3H, s), 2.39(3H, s), 1.46 (2H, m), 1.30 (2H, m), 0.89 (3H, t, J = 7.4 Hz).

Example 50: 2-Butylamino-8-hydroxy-9-(1-naphthylmethyl)adenine

[0105] The title compound was obtained in the same manner as in Example 11 using the compound obtained in Reference Example 5.
^{1}H NMR (DMSO-d_6) δ 9.79 (1H, s), 8.39-8.41 (1H, m), 7.94-7.97 (1H, m), 7.83-7.86 (1H, m), 7.55-7.59 (2H, m), 7.40-7.46 (1H, m), 7.26 (1H, m), 6.17 (1H, t, J = 5.8 Hz), 6.05 (2H, s), 5.28 (2H, s), 3.09-3.16 (2H, m), 1.36-1.44 (2H, m), 1.21-1.29 (2H, m), 0.83 (3H, t, J = 7.4 Hz)

Example 51: 2-Butylamino-8-hydroxy-9-(2-naphthylmethyl)adenine

[0106] The title compound was obtained in the same manner as in Example 11 using the compound obtained in Reference Example 5.
^{1}H NMR (DMSO-d_6) δ 9.69 (1H, s), 7.84-7.89 (3H, m), 7.74 (1H, s), 7.47-7.52 (3H, m), 6.21 (1H, t, J = 5.8 Hz), 6.03 (2H, s), 4.97 (2H, s), 3.12-3.20 (2H, m), 1.41-1.46 (2H, m), 1.22-1.31 (2H, m), 0.83 (3H, t, J = 7.4 Hz)

Example 52: 2-Butoxy-8-hydroxy-9-(1-naphthylmethyl)adenine

[0107] The title compound was obtained in the same manner as in Example 1 using a corresponding starting material.
^{1}H NMR (DMSO-d_6) δ 10.21 (1H, s), 8.37-8.41 (1H, m), 7.85-7.98 (2H, m), 7.55-7.60 (2H, m), 7.41-7.47 (1H, m), 7.25-7.28 (1H, m), 6.52 (2H, s), 5.34 (2H, s), 4.10 (2H, d, J = 6.6 Hz), 1.55-1.61 (2H, m), 1.29-1.38 (2H, m), 0.87 (3H, t, J = 7.3 Hz)

Example 53: 2-Butoxy-8-hydroxy-9-(2-naphthylmethyl)adenine

[0108] The title compound was obtained in the same manner as in Example 1 using a corresponding starting material.
^{1}H NMR (DMSO-d_6) δ 10.12 (1H, s), 7.87-7.90 (3H, m), 7.76 (1H, s), 7.46-7.51 (3H, m), 6.45 (2H, s), 5.02 (2H, s), 4.14 (2H, d, J = 6.6 Hz), 1.55-1.63 (2H, m), 1.31-1.39 (2H, m), 0.88 (3H, t, J = 7.3 Hz)

Example 54: 2-Butylamino-8-hydroxy-9-(5-chloro-2-thienylmethyl)adenine

[0109] The title compound was obtained in the same manner as in Example 11 using the compound obtained in Reference Example 5.
^{1}H NMR (DMSO-d_6) δ 9.85 (1H, s), 6.96 (1H, d, J = 3.8 Hz), 6.91 (1H, d, J = 3.8 Hz), 6.23 (1H, t, J = 5.4 Hz), 6.07 (2H, s), 4.87 (2H, s), 3.15-3.23 (2H, m), 1.43-1.53 (2H, m), 1.24-1.37 (2H, m), 0.89 (3H, t, J = 7.3 Hz)

Example 55: 2-Butylamino-8-hydroxy-9-(6-methyl-3-pyridylmethyl)adenine monosulfate

[0110] 0.5N sulfuric acid (30.8 ml) was added to a methanol solution (520 ml) of the compound of Example 27 (2.52 g, 7.70 mmol), and the precipitated crystal was collected by filtration. Thus, the title compound was obtained.

mp: 249-252°C				
Calc.	C 45.17,	H 5.45,	N 23.04,	S 7.54
Anal.	C 44.96,	H 5.56,	N 22.90,	S 7.53

Example 56: Interferon-inducing activity in mouse spleen cell (*in vitro*)

[0111] Spleen was extirpated from a C3H/HeJ mouse strain (male, 8 to 10 weeks old), and $2x10^6$ cells/ml of a splenic cell suspension was prepared using MEM medium containing 5% FBS. The resulting suspension was fractionated to each well of a 24-well microplate in amounts of 0.5 ml each. Thereafter, a test compound (comprising 0.2% DMSO) that was diluted in the same medium was added to each well in amounts of 0.5 ml each, and culture was conducted in an incubator in the presence of 5% CO_2 at 37°C for 24 hours. The culture solution was aseptically filtered through a 0.2-μm filter to obtain a culture supernatant. The interferon titer in the culture supernatant was quantified by the bioassay described in J. A. Armstrong, Methods in Enzymology 78, 381-7. More specifically, $1x10^4$ cells/50 μl of mouse fibroblasts, L929, were cultured in a 96-well culture plate for 24 hours, and 50 μl of diluted culture supernatant was added thereto, followed by culturing for an additional 24 hours. Subsequently, 100 μl each of vesicular stomatitis virus was added, and the cytopathogenic effect 44 hours after the virus infection was confirmed by crystal violet staining. Quantification was carried out by dissolving the dye with the aid of an aqueous solution of 2% sodium deoxycholate and assaying the absorbance at 595 nm. 9-Benzyl-2-butylamino-8-hydroxyadenine (a compound described in Example 24 of WO 99-28321) as Reference Compound 1, 9-benzyl-2-butoxy-8-hydroxyadenine (a compound described in Example 19 of WO 99-28321) as Reference Compound 2, R-837 (Imiquimod) as Comparative Example 1, and R-848 (1-(2-hydroxy-2-methylpropyl)-2-methoxyethyl-1H-imidazo[4,5-c]quinoline-4-amine) as Comparative Example 2 were used. Table 2 shows the minimum effective concentration of each compound.

Table 2

			Interferon-inducing activity
Compound	Minimum effective concentration (nM)	Compound	Minimum effective concentration (nM)
Example 1	1	Example 18	10
Example 2	1	Example 19	3
Example 3	1	Example 20	30
Example 4	10	Example 21	3
Example 5	3	Example 22	10
Example 6	1	Example 23	10
Example 7	1	Example 24	3
Example 8	1	Example 25	1
Example 9	3	Example 26	1
Example 10	10	Example 27	3
Example 11	3	Example 28	10
Example 12	10	Example 29	10
Example 13	3	Reference Compound 1	100
Example 14	1	Reference Compound 2	1
Example 15	1	Comparative Example 1	300
Example 16	1	Comparative Example 2	3
Example 17	3		

Example 57: Interferon-inducing activity in mouse (*in vivo*)

[0112] A test compound was suspended in an aqueous solution of 0.5% carboxymethylcellulose, and the resulting suspension was orally administered to a Balb/c male mouse. Two hours later, blood was sampled from its heart, and the interferon titer in blood serum was assayed in the same manner as in Example 56. Table 3 shows the results.

Table 3

	Interferon-inducing activity (U/ml)			
	Dosage (mg/kg)			
	0.01	0.03	0.1	0.3
Example 1		123±87	322±95	623±32
Example 2	25±17	388±87	1211±263	2559±495
Example 3			353±73	1966±532
Example 5			133±33	473±9
Example 6			569±42	1222±248
Example 7			347±149	845±22
Example 8	13±5	167±97	725±141	936±438
Example 9				539±107
Example 10		89±22	409±267	733±256
Example 11			279±177	568±160
Example 12				31±5
Example 13				304±138
Example 14				570±63
Example 15			52±32	603±147
Example 16			251±46	716±155
Example 17		31±23	183±43	999±379
Example 18				94±49
Example 19	14±5	199±84	383±122	601±187
Example 21		15±8	290±134	571±164
Example 22			21±9	332±83
Example 23			42±7	414±118
Example 24				403±146
Example 25	65±52	151±29	753±140	721±299
Example 26		121±11	433±366	780±190
Example 27		14±3	324±66	804±274
Example 28			186±62	1462±260
Example 29				619±268
Reference Compound 1			55±25	275±165
Reference Compound 2		60±40	186±42	317±160
Comparative Example 2			1638±246	1961±950

Example 58: Interferon-inducing activity in cynomolgus monkey (*in vivo*)

[0113] A test compound was suspended in an aqueous solution of 0.5% carboxymethylcellulose, and 10 mg/kg of the resulting suspension was orally administered to a group of five male cynomolgus monkeys. Blood was sampled with the elapse of time, and the interferon titer in blood serum was assayed in the same manner as in Example 56. The interferon titers in blood serum four hours after the administration (average ± SE) were 13,876±825 U/ml in the compound of Example 17, 12,173±6619 U/ml in the compound of Example 19, 14,488±6365 U/ml in the compound of Example 27, and 18,305 ± 5578 U/ml in the compound of Reference Example 2. These results indicate that interferon-inducing activity of each case was substantially the same. While vomition was observed in 4 out of 5 samples in the compound of Reference Example 2, no vomition was observed in any sample in the case of the compound according to the present invention.

Example 59: Interferon-inducing activity in human peripheral blood mononuclear cells (PBMC)

[0114] Peripheral bloods were sampled from 5 healthy volunteers using a syringe containing heparin, and peripheral blood mononuclear cells (PBMC) were prepared by density gradient centrifugation utilizing the Lymphoprep™ (NYCOMED PHARMA AS). PBMCs were washed twice in serum-free RPMI 1640 medium and adjusted at $1x10^6$ cells/ml in RPMI 1640 medium comprising 10% fetal bovine serum. The product was cultured in the presence of a test compound dissolved in dimethyl sulfoxide (final concentration: 0.1%) in an incubator in the presence of 5% CO^2 at 37°C for 24 hours. As a control, 0.1% dimethyl sulfoxide containing no test compound was used. The culture supernatant was aseptically collected by filtration. Thereafter, the supernatant was cryopreserved at -20°C or lower until it was subjected to the assay for IFN-inducing activity. Human IFN-α in the culture supernatant was quantified using a highly sensitive ELISA system (Amersham). Table 4 shows the results, wherein (-) indicates a detection limit (1.25 pg/ml) or lower and NT refers to "not tested."

Table 4

Interferon-inducing activity (pg/ml)					
	Concentration (nM)				
	0.3	1	3	10	30
Example 17	NT	5±3	17±17	50±33	61±38
Example 19	NT	5±1	12±11	48±34	60±33
Example 25	7±3	28±24	46±34	NT	NT
Example 27	NT	6±3	26±22	56±37	59±33
Comparative Example 2	-	-	6±5	NT	NT
Reference Compound 2	NT	-	7	23±22	64±40

Example 60: Inhibitory activity against Th2 cytokine produced from sensitized spleen cells

[0115] A 7-week-old BALB/c mouse was immunized intraperitoneally with aluminum hydroxide gel (4 mg, 100 μl) having 10 μg of ovalbumin adsorbed thereon, and it was subjected to additional immunization with the same agent 14 days later. Seven days thereafter, spleen was taken out, and suspended in RPMI-1640 comprising inactivated fetal bovine serum (10%), 2-mercaptoethanol (50 μl), penicillin G (100 U/ml), and streptomycin (100 μg/ml). Thus, a splenic cell suspension was prepared. Ovalbumin (0.5 mg/ml) and a test compound were added to a splenic cell suspension ($5x10^6$ cell/200 μl/well), and the resultant was cultured at 37°C in the presence of 5% CO_2 for 3 days. The cytokine level in the culture supernatant was quantified by ELISA. IFN-γ and IL-4 were assayed using a kit available from Amersham, and IL-5 was assayed using a kit available from Endogen. Table 5 shows the results.

Table 5

Inhibitory activity against IL-4 production (% of control)				
	Concentration (nM)			
	0.1	1	10	100
Example 1	98	7	2	<1

Table 5 (continued)

Inhibitory activity against IL-4 production (% of control)				
	Concentration (nM)			
	0.1	1	10	100
Example 2	96	4	<1	<1
Example 10	-	54	3	<1
Example 17	-	40	<1	<1
Example 19	-	32	<1	<1
Example 20	-	106	23	2
Example 21	-	53	1	<1
Example 22	-	88	9	1
Example 25	86	2	<1	<1
Example 27	-	30	1	<1
Comparative Example 1	-	18	1	< 1
Comparative Example 2	90	24	1	<1
Reference Compound 1	-	-	109	24
Reference Compound 2	107	48	1	<1

Inhibitory activity against IL-5 production (% of control)				
	Concentration (nM)			
	0.1	1	10	100
Example 1	116	41	16	15
Example 2	98	37	14	12
Example 10	-	91	32	15
Example 17	-	77	24	10
Example 19	-	83	16	13
Example 20	-	106	71	19
Example 21	-	97	23	15
Example 22	-	115	50	18
Example 25	102	31	13	13
Example 27	-	68	20	12
Comparative Example 1	-	54	15	10
Comparative Example 2	106	73	18	10
Reference Compound 1	-	-	92	69
Reference Compound 2	99	79	16	11

Example 61: Gastrointestinal absorption in rat

[0116] A test compound was suspended in an aqueous solution of 0.5% carboxymethylcellulose, and the resulting suspension was orally administered to an SD male rat. Blood was sampled with the elapse of time, and the level of the drug in blood was assayed by HPLC. The following table shows the Cmax and Tmax values.

Table 6

Cmax and Tmax			
	Dose (mg/kg)	Cmax (ng/ml)	Tmax (hr)
Example 17	3	310	1
Example 19	3	188	4
Hydrochloride of Example 25	3 10	18 150	1 0.25
Example 27	3	565	0.5
Comparative Example 1	3	90	0.5
Comparative Example 2	3 10	19 15	1 0.5

Example 62: Solubility

[0117] 5.53% citric acid (monohydrate) and 1.75% disodium phosphate (anhydrous) were mixed together to prepare buffers (pH 2.5, 5.5, 7.4). A compound was added thereto, the mixture was stirred in a vortex mixer and subjected to ultrasonication for 30 minutes. Thereafter, the resultant was stirred in a vortex mixer again and then centrifuged at 15,000 rpm for 20 minutes. The levels of the compounds in the supernatants were then quantified by HPLC. The following table shows these concentration levels.

Table 7

			(μg/ml)
	pH 2.5	pH 5.5	pH 7.4
Example 8	784	20	18
Example 9	350	4	3
Example 10	34	15	10
Example 15	140	1	< 1
Example 16	293	NT	NT
Example 19	130	2	2
Example 20	8,813	NT	NT
Example 21	15,000	45	64
Example 22	> 80,000	73	16
Example 24	27,000	22	1
Example 25	> 1,000	5	3
Example 26	> 1,000	6	3
Example 27	610	5	2
Example 28	> 1,000	8	4
Example 31	> 1,000	353	322
Example 32	> 1,000	82	25
Reference Compound 1	26	< 1	< 1
Reference Compound 2	2	< 1	< 1

Example 63: Medicinal effect of the compound of Example 27 in a rat model of eosinophil leukocytic infiltration

[0118] A rat was immunized intraperitoneally with 1 ml of a solution containing 1 mg of ovalbumin (OVA) and 100

mg of $Al(OH)_3$ on day 0 and day 7. On day 14, a 1% OVA solution was sprayed for 15 minutes using a ultrasonic nebulizer to induce reactions. A test compound was administered intratracheally 2.5 hours before the induction. Bronchoalveolar lavage was performed 24 hours after the induction, and eosinocytes in the wash was stained with Hinkelman to count the number of stained cells. Sensi.-/Challe.+, CMC-Na, and Fluticasone were used as controls. Fig. 1 and the following table show the results.

Table 8

	x 10^4 cells		
Compound (intratracheal administration)	Average	Standard deviation	Standard error
Sensi.-/Challe.+	26.22	15.60	6.37
CMC-Na	319.55	281.89	115.08
Example 27 (0.001 mg/kg)	383.85	392.01	160.04
Example 27 (0.01 mg/kg)	186.77	161.86	66.08
Example 27 (0.1 mg/kg)	46.84	51.84	21.16
Fluticasone (0.01 mg/kg)	300.07	231.84	94.65

Example 64: Medicinal effect of the compound of Example 17 in a mouse model of active cutaneous anaphylaxis

[0119] A mouse was immunized intraperitoneally with 500 μl of a solution containing 2 μg of ovalbumin (OVA) and 5 mg of $Al(OH)_3$ on day 0. On day 14, 20 μl of 1 mg/ml OVA solution was intradermally injected in the left auricle under ether anesthesia to induce the reaction. A test compound was applied to both surfaces of the left auricle in amounts of 10 μl each 2 hours before the induction. The thickness of the auricle was measured using a micrometer 24 hours after the induction. Acetone was used as a control. Fig. 2 and the following table show the results.

Table 9

	Ear swelling (mm)		
Compound	Average	Standard deviation	Standard error
Acetone	0.034	0.021	0.009
Example 17 (4 μg/ear)	0.046	0.024	0.010
Example 17 (40 μg/ear)	0.048	0.013	0.005
Example 17 (400 μg/ear)	0.014	0.008	0.003

Example 65: Antitumor effect of the compound of Example 27 in tumor-bearing mouse model

[0120] Murine renal adenocarcinoma-derived Renca cells (obtained from Iwate Medical University) were intradermally transplanted to the left ventral portions of 6-week-old BALB/c male mice (Charles River Japan, Inc.) at $5x10^4$ cells/0.05 ml/mouse. Their body weights were measured on the next day, and they were divided into 5 groups (each group comprising 6 mice) in such a manner that the average body weights were substantially the same among groups. Vehicles (an aqueous solution of 0.5% carboxymethylcellulose (hereinafter referred to as "CMC-Na")) and the compound of Example 27 (1 mg/kg and 3 mg/kg) were forcibly administered orally using an oral Sonde (10 ml/kg). Mouse interferon α (hereinafter referred to as "mIFN-α") was intradermally administered to mice through their backs in amounts of $1x10^4$ U/0.1 ml and $5x10^4$ U/0.1 ml per mouse. Administration was carried out 5 times every 4 days. The longer diameter (L, mm) and the shorter diameter (W, mm) of the generated tumors were measured twice a week, and the tumor volumes (V, mm^3) were calculated ($V=L\times W^2$). Also, significant difference was examined in accordance with Steel's multiple comparison. The SAS system for Windows Release 8.01 (SAS Institute Inc., Cary, NC, U.S.A.) was used for the examination.

[0121] A surveillance period of about 30 days after the transplantation was provided, the tumor volume and the body weight were monitored, and an antitumor effect against the Renca cells was evaluated. The average tumor volume (n = 6) of each agent was compared with those of cases involving vehicle administration. The results thereof are shown in Fig. 3. As a result, the tumor volume in the groups to which the compound of Example 27 and mIFN-α were administered was significantly smaller than that in the group to which vehicles had been administered (P <0.05). Adminis-

tration of the compound of Example 27 was found to exhibit the antitumor effect equivalent to or higher than that attained by the administration of mIFN-α.

Example 66: Antitumor effect of the compound of Example 27 in a mouse model of spontaneous metastasis (inhibitory effect against metastasis)

[0122] OV2944-HM-1 cells (obtained from Hiroshima University) derived from mouse ovarian cancer that is highly metastatic to the lymph nodes were intradermally transplanted to the buttocks of 6-week-old B6C3F1 female mice (Charles River Japan, Inc.) in amounts of $1x10^6$ cells/0.05 ml/mouse. Ten days after the transplantation, the primary tumor was excised under Nembutal anaesthesia. Adhesives (Aron Alpha) were applied to the excised portions, and the stumps were sewed up with wound clips. The next day, body weights were measured, and they were divided into 3 groups (each group comprising 6 mice) in such a manner that the average body weights among groups were substantially the same. Vehicles (aqueous solutions of 0.5% CMC-Na) and the compound of Example 27 (3 mg/kg) were forcibly administered orally using an oral Sonde (10 ml/kg). Also, $5x10^4$ U/0.1 ml/mouse of mIFN-α was intradermally administered through their backs. Administration was carried out 5 times every 4 days. Regional lymph nodes (mouse cervical, brachium, axillary cavity) were extirpated 35 days after the transplantation, and their wet weights were measured. Simultaneously, lungs were extirpated to visually inspect the metastasis. Also, significant difference was examined in accordance with Steel's multiple comparison. The SAS system for Windows Release 8.01 (SAS Institute Inc., Cary, NC, U.S.A.) was used for the examination.

[0123] As shown in Fig. 4, the largest metastatic focus was the mouse cervical lymph node located close to the primary tumor, followed by the axillary cavity lymph node and brachium lymph node. The weight of each metastasis lymph node of the group to which the compound of Example 27 was administered was smaller than those attained from the group to which vehicles were administered. This indicates that the compound of Example 27 exhibits a metastasis-inhibiting effect. The HM-1 cells exhibit not only lymph node metastasis but also highly frequent pulmonary metastasis. Thus, pulmonary metastasis was examined. As shown in the table below, pulmonary metastasis was observed in 5 out of 6 mice in the group to which vehicles had been administered based on visual inspection; however, it was not observed at all with the administration of the compound of Example 27. This indicates that the compound of Example 27 can potently inhibit pulmonary metastasis in addition of its ability to inhibit lymph node metastasis. In contrast, mIFN-α did not inhibit lymph node metastasis, and the frequency of pulmonary metastasis was the same as that attained in the group to which vehicles had been administered.

Table 10

	The number of mice which exhibited pulmonary metastasis in 6 mice
Vehicle	5
Mouse interferon α	5
Compound of Example 27	0

Example 67: Preparation Example

[0124] Tablets having the following composition were produced in accordance with a conventional technique.

Compound of Example 25	10 mg
Lactose	600 mg
Starch	250 mg
Hydroxypropylcellulose	30 mg
Calcium stearate	5 mg

Example 68: Preparation Example

[0125] Solid dispersants having the following composition were produced in accordance with a conventional technique.

Compound of Example 27	20 mg
Nikkol (surfactant)	5 mg

(continued)

Hydroxypropylcellulose	200 mg
Methanol	2 ml
Dichloromethane	2 ml

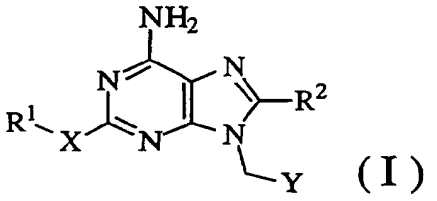
[0126] All publications cited herein are incorporated herein by reference in their entirety.

Industrial Applicability

[0127] The adenine derivative according to the present invention has selective and significant interferon-inducing activity. The adenine derivative according to the present invention accelerates interferon secretion in living organisms, and thus, is useful for prevention or treatment of, for example, viral diseases such as hepatitis B, hepatitis C, or AIDS or cancerous diseases for which interferon is effective. The adenine derivative according to the present invention is of low molecular weight. Accordingly, it can be orally administered, unlike interferon preparations. In addition, the adenine derivative according to the present invention is a compound having excellent water solubility and high gastrointestinal absorption. Further, the adenine derivative according to the present invention selectively inhibits the production of inflammatory cytokines such as IL-4 or IL-5 that are discharged from Th2 cells. Accordingly, it is useful as a preventive or therapeutic agent for diseases such as asthma or atopic dermatitis with which Th2 cells are deeply involved.

Claims

1. An adenine derivative, a tautomer thereof, or a pharmaceutically acceptable salt thereof represented by general formula (I):



(I)

wherein X represents NR^3 (wherein R^3 represents a hydrogen atom or C_{1-3} alkyl), an oxygen atom, or a sulfur atom; R^1 represents substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl; R^2 represents hydroxyl, mercapto, C_{1-8} acyloxy, or C_{2-8} alkoxycarbonyloxy; and Y represents a substituted or unsubstituted naphthalene ring, a substituted or unsubstituted 5- or 6-membered monocyclic aromatic hetero ring containing 1 or 2 hetero atoms selected from the group consisting of nitrogen, oxygen, and sulfur atoms, or a substituted or unsubstituted fused bicyclic aromatic hetero ring containing 1 or 2 hetero atoms selected from the group consisting of nitrogen, oxygen, and sulfur atoms.

2. The compound according to claim 1, wherein, in general formula (I), R^1 represents C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{2-8} alkoxyalkyl, C_{1-8} hydroxyalkyl, aryl, heteroaryl, aralkyl, or heteroarylalkyl.

3. The compound according to claim 1, wherein, in general formula (I), R^1 represents C_{1-6} alkyl.

4. The compound according to claim 1, wherein, in general formula (I), X represents NH.

5. The compound according to claim 1, wherein, in general formula (I), X represents an oxygen atom.

6. The compound according to claim 1, wherein, in general formula (I), Y represents a unsubstituted or substituted pyridine ring or a substituted or unsubstituted pyrazine ring.

7. The compound according to claim 1, wherein, in general formula (I), Y represents a unsubstituted or substituted naphthalene ring or a substituted or unsubstituted thiophene ring.

8. The compound according to claim 1, wherein, in general formula (I), Y has 1 to 4 substituents when Y is a pyridine ring, and 1 to 3 substituents when Y is a pyrazine ring at any positions, wherein the substituent is selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, hydroxyl, mercapto, C_{1-4} alkylthio, a halogen atom, amino, C_{2-8} dialkylamino, C_{1-4} monoalkylamino, pyrrolidinyl, piperidino, and morpholino.

9. The compound according to claim 1, wherein, in general formula (I), Y represents a pyridine ring which may have a substituent selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, hydroxyl, mercapto, C_{1-4} alkylthio, a halogen atom, amino, C_{2-8} dialkylamino, C_{1-4} monoalkylamino, pyrrolidinyl, piperidino, and morpholino; R^1 represents C_{1-6} alkyl; and R^2 represents hydroxyl.

10. The compound according to claim 9, wherein X represents NH or an oxygen atom.

11. A pharmaceutical comprising, as an active ingredient, the compound according to any one of claims 1 to 10.

12. An interferon inducer comprising, as an active ingredient, the compound according to any one of claims 1 to 10.

13. An antiviral agent comprising, as an active ingredient, the compound according to any one of claims 1 to 10.

14. An anticancer agent comprising, as an active ingredient, the compound according to any one of claims 1 to 10.

15. A type 2 helper T cell selective immune response inhibitor comprising, as an active ingredient, the compound according to any one of claims 1 to 10.

16. An antiallergic agent comprising, as an active ingredient, the compound according to any one of claims 1 to 10.

17. An immune response modulator comprising, as an active ingredient, the compound according to any one of claims 1 to 10.

Fig. 1

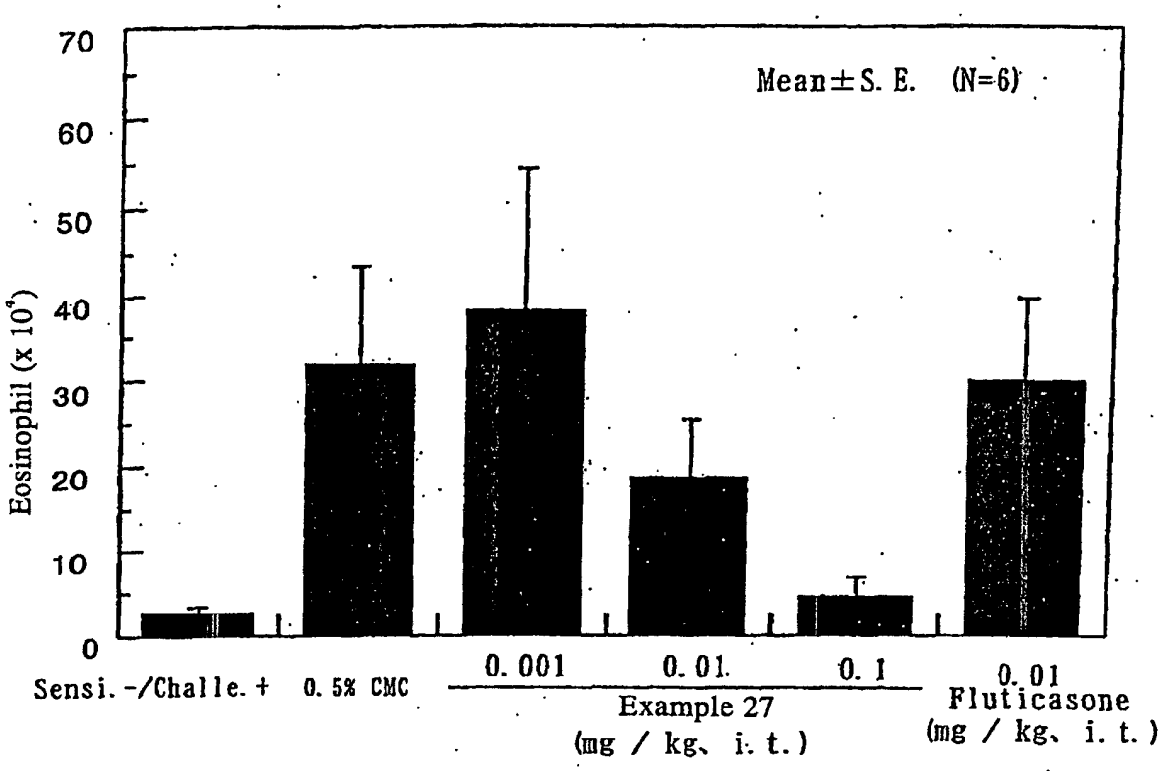

70
60
50
40
30
20
10
0
Eosinophil (x 10⁴)
Mean±S. E. (N=6)
Sensi. -/Challe. +
0. 5% CMC
0. 001
0. 01
0. 1
Example 27
(mg / kg, i. t.)
0. 01
Fluticasone
(mg / kg, i. t.)

Fig. 2

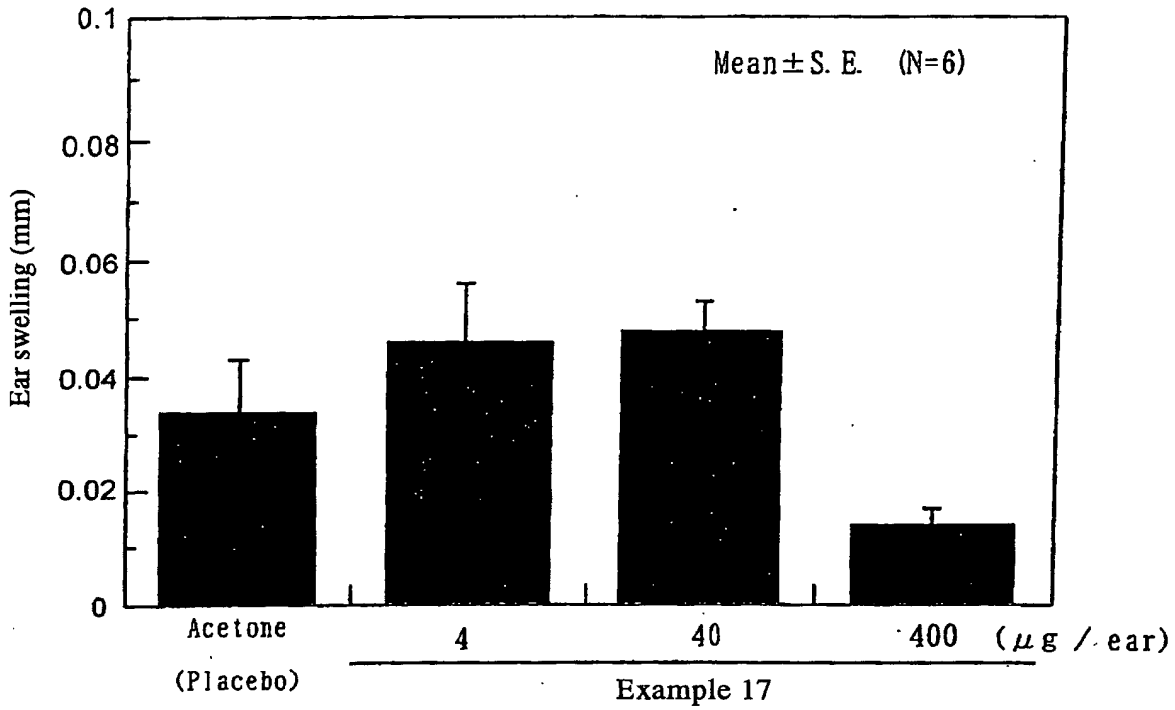

0.1
0.08
0.06
0.04
0.02
0
Ear swelling (mm)
Mean±S. E. (N=6)
Acetone
(Placebo)
4
40
400
(μg / ear)
Example 17

Fig. 3

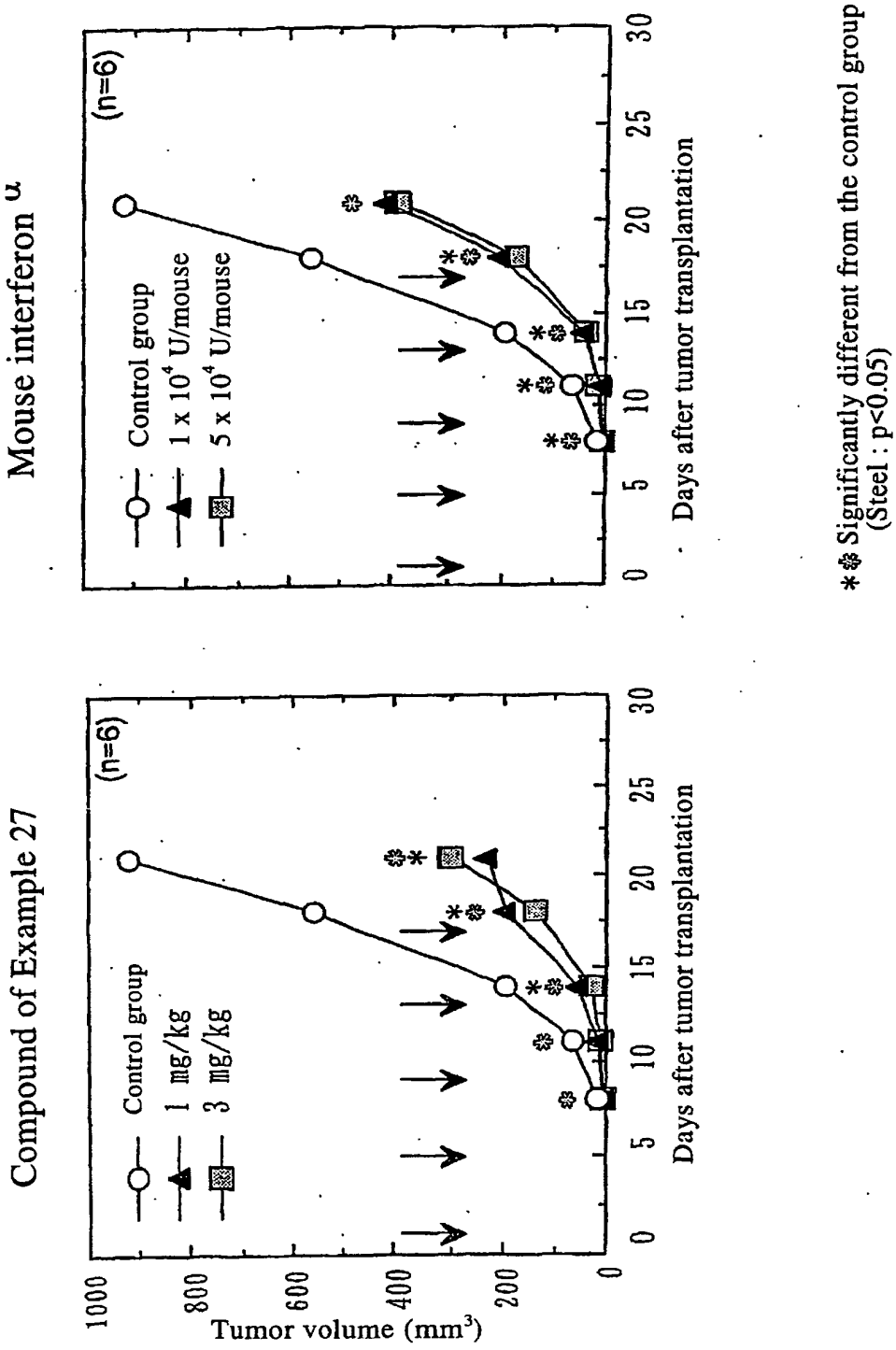
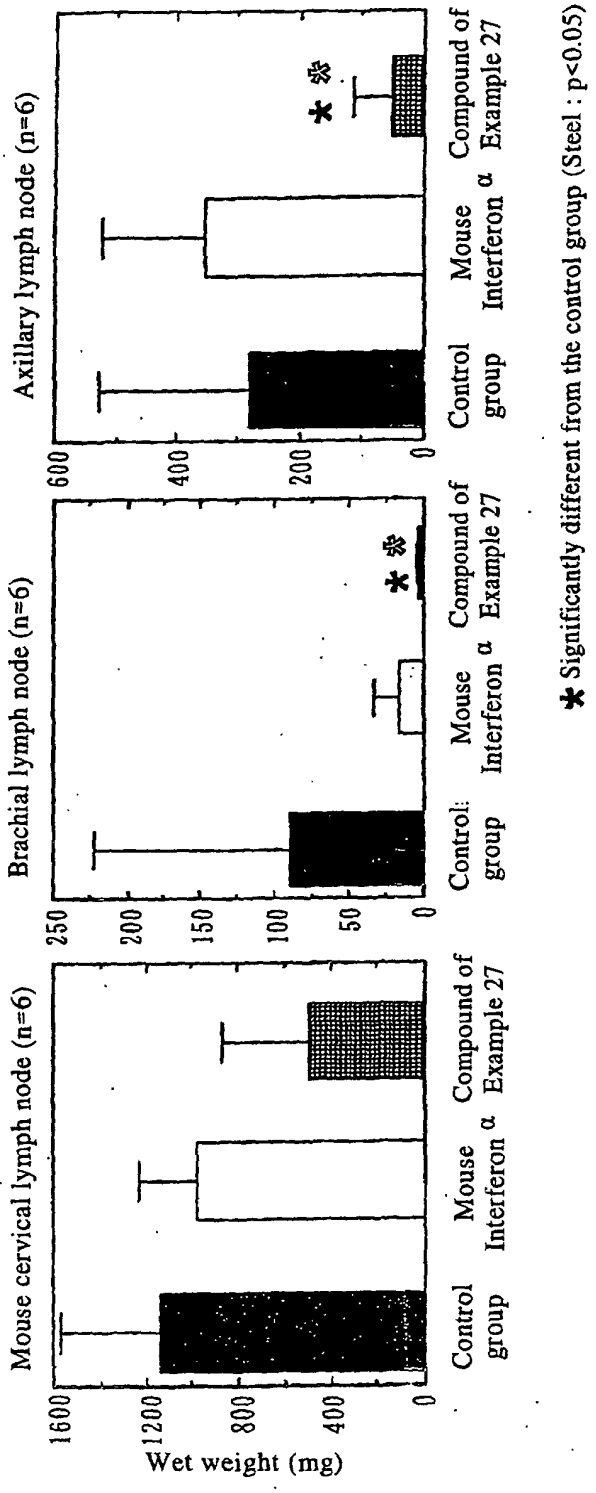

Compound of Example 27
Mouse interferon α
(n=6)
Control group
1 mg/kg
3 mg/kg
1 x 10^4 U/mouse
5 x 10^4 U/mouse
Tumor volume (mm^3)
Days after tumor transplantation
* * Significantly different from the control group
(Steel : p<0.05)

Fig. 4


Mouse cervical lymph node (n=6)
Brachial lymph node (n=6)
Axillary lymph node (n=6)
Wet weight (mg)
1600
1200
800
400
0
250
200
150
100
50
0
600
400
200
0
Control group
Mouse Interferon α
Compound of Example 27
✱ Significantly different from the control group (Steel : p<0.05)
✱✱ Significantly different from the mouse interferon α-administered group (Steel : p<0.05)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP02/03727

A. CLASSIFICATION OF SUBJECT MATTER
Int.Cl[7] C07D473/16, 473/18, 473/24, A61K31/52, A61P11/06, 17/00, 31/12, 31/18, 31/20, 35/00, 37/02, 37/06, 37/08, 43/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
Int.Cl[7] C07D473/16, 473/18, 473/24, A61K31/52

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
REGISTRY(STN), CAPLUS(STN), CAOLD(STN)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 1035123 A1 (Sumitomo Pharmaceuticals Co., Ltd.), 13 September, 2000 (13.09.00), & WO 99/28321 A1 & CA 2311742 A & AU 9912602 A1 & US 6329381 B1	1-17
A	JP 11-193282 A (Sumitomo Pharmaceuticals Co., Ltd.), 21 July, 1999 (21.07.99), (Family: none)	1-17
A	JP 48-16519 B1 (Tanabe Seiyaku Co., Ltd.), 22 May, 1973 (22.05.73), (Family: none)	1-3

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
03 July, 2002 (03.07.02)	16 July, 2002 (16.07.02)
Name and mailing address of the ISA/ Japanese Patent Office	Authorized officer
Facsimile No.	Telephone No.

Form PCT/ISA/210 (second sheet) (July 1998)

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 605 836 A1**

(12) **EUROPEAN PATENT APPLICATION**

(21) Application number: **93120533.0**

(51) Int. Cl.5: **C07D 501/36**, A61K 31/545

(22) Date of filing: **20.12.93**

(30) Priority: **18.12.92 JP 339267/92**
03.08.93 JP 192403/93

(43) Date of publication of application:
13.07.94 Bulletin 94/28

(84) Designated Contracting States:
DE ES FR GB IT

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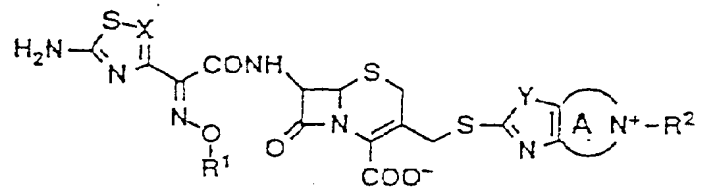
(54) **Cephalosporin derivatives.**

(57) A cephalosporin derivative having a quaternary salt type substituent group at the 3-position, represented by formula (I):



(I)

wherein X is a carbon atom or a nitrogen atom; Y is a sulfur atom, an oxygen atom or a nitrogen atom substituted with a substituted or unsubstituted lower alkyl group; R^1 is a hydrogen atom, a lower alkyl group or a substituted lower alkyl group; R^2 is a lower alkyl group, a substituted lower alkyl group, a lower alkylene group or a substituted lower alkylene group; and A is an unsaturated six-membered heterocyclic ring containing at least one nitrogen atom, or a pharmaceutically acceptable salt thereof is disclosed. The derivatives have excellent antibacterial activities and can be used as a drug for the treatment of various bacterial infections.

EP 0 605 836 A1

FIELD OF THE INVENTION

This invention relates to novel cephalosporin derivatives which have a quaternary salt type substituent group at the 3-position. More particularly, it relates to cephalosporin derivatives which have a strong antibacterial activity and a broad antibacterial spectrum.

BACKGROUND OF THE INVENTION

Cephalosporin antibiotics are markedly effective drugs for the treatment of infectious diseases in mammals in view of their excellent antibacterial activities and low toxicity against mammals. In recent years, a number of cephalosporin derivatives having an aminothiazolylacetyl group at the 7-position of the cephem ring have been studied and developed since they show strong antibacterial activities and high stability against β-lactamase.

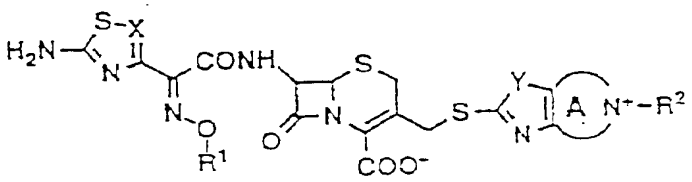
In various countries, many studies have addressed so-called "onium salt type cephalosporin antibiotics" such as ceftazidime and cefpirome which have an aminothiazolylacetyl group and a quaternary salt type substituent group at the 7-position and the 3-position, respectively and exert strong antibacterial activities and broad antibacterial spectrum ranging from gram-positive bacteria to *Pseudomonas aeruginosa*. However, these onium salt type cephalosporin antibiotics including ceftazidime and cefpirome are still unsatisfactory in terms of their antibacterial activities upon *Pseudomonas aeruginosa* and gram-positive bacteria including *Staphylococcus aureus* which have recently been given attention in a clinical viewpoint. Thus, great concern has been directed toward the development of novel cephalosporin antibiotics having improved antibacterial activities upon these bacteria.

SUMMARY OF THE INVENTION

An object of the present invention is to provide novel cephalosporin derivatives having strong antibacterial activities on various pathogenic bacteria.

The present inventors have conducted intensive studies in order to develop novel cephalosporin derivatives which have strong antibacterial activities and broad antibacterial spectrum. As a result, the inventors have succeeded in synthesizing novel cephalosporin derivatives represented by the following formula (I) which exhibit excellent antibacterial activities and broad antibacterial spectrum.

Thus, the present invention provides a cephalosporin derivative represented by formula (I):



(I)

wherein X is a carbon atom or a nitrogen atom; Y is a sulfur atom, an oxygen atom or a nitrogen atom substituted with a substituted or unsubstituted lower alkyl group; R^1 is a hydrogen atom, a lower alkyl group or a substituted lower alkyl group; R^2 is a lower alkyl group, a substituted lower alkyl group, a lower alkylene group or a substituted lower alkylene group; and A is an unsaturated six-membered heterocyclic ring which contains at least one nitrogen atom, or a salt thereof.

The present invention further provides an antibacterial composition comprising the cephalosporin derivative or a pharmaceutically acceptable salt thereof as an active ingredient and a pharmaceutically acceptable carrier.

DETAILED DESCRIPTION OF THE INVENTION

In the definition of formula (I), the term "lower alkyl group" or "lower alkylene group" means a straight or branched alkyl or alkylene group having 1 to 4 carbon atoms. Specific examples of substituent groups in the substituted lower alkyl and lower alkylene groups in formula (I) include a halogen atom (fluorine, chlorine, bromine or iodine), a hydroxyl group, a carboxyl group, a carbamoyl group, an amino group, a lower alkylamino group having 1 to 4 carbon atoms and these groups substituted with a lower alkyl group

having 1 to 4 carbon atoms, a lower alkylene group having 1 to 4 carbon atoms, an aralkyl group having 7 to 10 carbon atoms and the like.

The A ring may contain other hetero atoms as long as it is an unsaturated six-membered heterocyclic ring which contains at least one nitrogen atom. Specific examples thereof include unsaturated heterocyclic rings having only nitrogen atom(s) as a hetero atom, such as pyridine ring, pyrimidine ring, pyrazine ring, pyridazine ring and their dihydro or tetrahydro derivatives, and other nitrogen atom-containing unsaturated heterocyclic rings further having sulfur, oxygen or the like hetero atom, such as thiazine ring, thiadiazine ring, oxazine ring, oxadiazine ring and the like.

Examples of the cephalosporin derivatives of the present invention represented by formula (I) are given below by way of illustration and not by way of limitation.

1. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(5-methylthiazolo[4,5-c]pyridinium-2-yl)-thiomethyl-3-cephem-4-carboxylate
2. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(4-methylthiazolo[4,5-b]pyridinium-2-yl)-thiomethyl-3-cephem-4-carboxylate
3. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-carboxymethoxyiminoacetamido}-3-(5-methylthiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
4. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido)-3-(5-methylthiazolo[4,5-c]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
5. 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(5-methylthiazolo[4,5-c]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
6. 7-{(Z)-2-(5-aminothiadiazol-3-yl)-2-methoxyiminoacetamido}-3-(5-methylthiazolo[4,5-c]pyridinium-2-yl)-thiomethyl-3-cephem-4-carboxylate
7. 7-{(Z)-2-(5-aminothiazol-3-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-(5-methylthiazolo[4,5-c]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
8. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-carboxymethoxyiminoacetamido}-3-(4-methylthiazolo[4,5-b]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
9. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-(4-methylthiazolo[4,5-b]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
10. 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(4-methylthiazolo[4,5-b]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
11. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(5-methylthiazolo[5,4-c]pyridinium-2-yl)-thiomethyl-3-cephem-4-carboxylate
12. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-carboxymethoxyiminoacetamido}-3-(5-methylthiazolo[5,4-c]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
13. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-(5-methylthiazolo[5,4-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
14. 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(5-methylthiazolo[5,4-c]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
15. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(4-methylthiazolo[5,4-b]pyridinium-2-yl)-thiomethyl-3-cephem-4-carboxylate
16. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-carboxymethoxyiminoacetamido}-3-(4-methylthiazolo[5,4-b]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
17. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-(4-methylthiazolo[5,4-b]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
18. 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(4-methylthiazolo[5,4-b]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
19. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(5-carboxymethylthiazolo[4,5-c]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
20. 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(5-ethylthiazolo[4,5-c]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
21. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-(5-ethylthiazolo[4,5-c]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
22. 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-{5-(2-fluoroethyl)thiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
23. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-{5-(2-fluoroethyl)-thiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate
24. 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-{5-(2-hydroxyethyl)thiazolo-[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

25. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-{5-(2-hydroxyethyl)-thiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

26. 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(5-carbamoylmethylthiazolo-[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

27. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-(5-carbamoylmethyl thiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

28. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(5-methyloxazolo[4,5-c]pyridinium-2-yl)-thiomethyl-3-cephem-4-carboxylate

29. 7-{(Z)-2-(2-aminothiazol-4-yl)-2-carboxymethoxyiminoacetamido}-3-(5-methyloxazolo[4,5-c)-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

30. 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(5-methyloxazolo[4,5-c]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

31. 7-{(Z)-2-(5-aminothiazol-3-yl)-2-methoxyiminoacetamido}-3-(5-(2-methyloxazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

32. 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(5-methylthiazolo[4,5-d]-pyridazinium-2-yl)thiomethyl-3-cephem-4-carboxylate

33. 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(5,5-dimethyl-4H,6H,7H-thiazolo[5,4-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

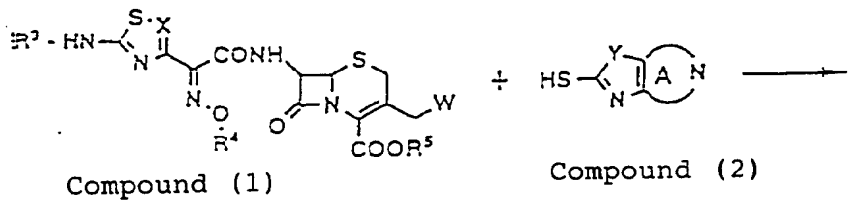
34. 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(1,5-dimethylimidazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

The compound of formula (I) of the present invention may be in the form of a pharmaceutically acceptable salt such as sodium, hydrochloride, sulfate or the like.

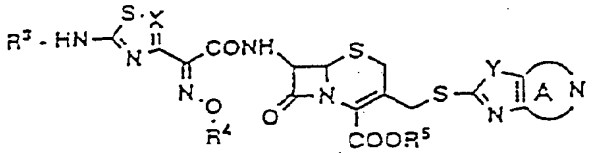
Though the compound of formula (I) of the present invention can be produced by various means, it is convenient to produce it in accordance with process (A) which comprises steps 1 to 3, process (B) which comprises steps (a) to (d) or process (C) which comprises steps i to ii, as diagrammatically shown below with respective reaction schemes.

Production process (A)

Step 1



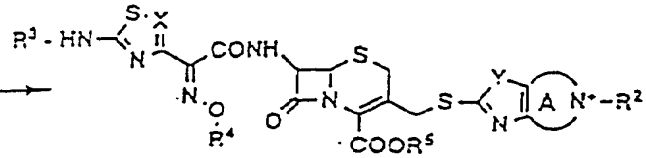
Compound (1) + Compound (2)



Compound (3)

Step 2

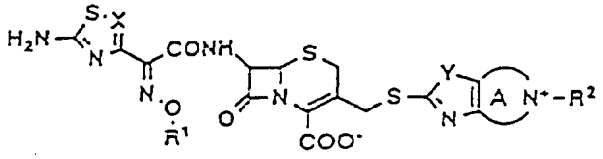
Compound (3) + R^2-W ⟶



Compound (4) Compound (5)

Step 3

Compound (5) ⟶



Compound (I)

In the compounds (1) to (5) and (I) shown in the above respective schemes, each of R^1, R^2, X and Y has the same meaning as described in formula (I) of the present invention.

The starting compound (1) can be synthesized in accordance with the method well known in the art as described in J. Antibiot., 44, 1371 (1991), ibid., 38, 1738 (1985), J. Med. Chem., 33, 77 (1990), JP-A-60-78987 and JP-A-58-222092 (the term "JP-A" used herein means an unexamined published Japanese patent application).

In the starting compound (1) to be used in the step 1 of the above production process (A), R^3 is an amino protective group such as a trityl group, a chloroacetyl group, a formyl group or the like, R^4 is the same group of R^1 or an oxime protective group such as a trityl group and R^5 is a carboxyl protective ester-

forming group such as a diphenylmethyl group, a benzyl group, a p-methoxybenzyl group, a p-nitrobenzyl group, a tert-butyl group, an allyl group, a 2,2,2-trichloroethyl group or the like. W in the starting compound (1) is a leaving group such as a halogen atom (chlorine, bromine or iodine), a diphenylphosphoryloxy group, a methanesulfonyloxy group, a p-toluenesulfonyloxy group, a trifluoromethanesulfonyloxy group or the like. The deprotection of the compound of formula (I) in which R^4 is an oxime protective group gives the compound of formula (I) in which R^1 is hydrogen.

The steps 1 to 3 of the production process (A) shown above can be carried out as follows.

In the step 1, a starting compound (1) is allowed to undergo a substitution reaction in an anhydrous organic solvent with a compound (2) or its sodium salt to obtain a compound (3). The molar ratio of the compound (2) to the compound (1) ranges from 1.1 to 2.0, preferably 1.2 to 1.5. Preferred examples of the reaction solvent include chloroform, dichloromethane, tetrahydrofuran, N,N-dimethylformamide, acetonitrile, hexamethylphosphate triamide and the like. The reaction may be effected at a temperature of preferably from -20 to 50 °C for 1 to 4 hours. After completion of the reaction, the reaction mixture is subjected to usual after-treatments comprising, for example, putting the reaction mixture into water, effecting extraction with a solvent into which the compound (3) can be dissolved, such as chloroform, dichloromethane or ethyl acetate, washing the organic layer with water, drying the organic layer with a drying agent and removing the solvent under reduced pressure. If necessary, the thus obtained compound (3) is purified by means of silica gel column chromatography, crystallization and the like.

In the step 2, the compound (3) is allowed to react with a compound (4) in an anhydrous organic solvent to obtain a compound (5) in which the nitrogen atom at the 3-position is made into a quaternary salt. The molar ratio of the compound (4) to the compound (3) ranges from 5 to 100, preferably 20 to 50. Preferred examples of the reaction solvent include benzene, toluene, chloroform, dichloromethane, tetrahydrofuran, N,N-dimethylformamide and the like, with benzene and N,N-dimethylformamide being particularly preferred. The reaction may be effected at a temperature of preferably from -20 to +50 °C, more preferably from 20 to 30 °C within 24 hours. After completion of the reaction, the reaction mixture is subjected to usual after-treatments and, if necessary, the thus obtained compound (5) is purified by means of silica gel column chromatography, Sephadex gel filtration, crystallization and the like.

In the step 3, protective groups R^3, R^4 and R^5 of the compound (5) are eliminated by deprotection to obtain the compound (I) of the present invention. The deprotection reaction for the elimination of the groups R^3, R^4 and R^5 may be carried out by usually used means in any optional order.

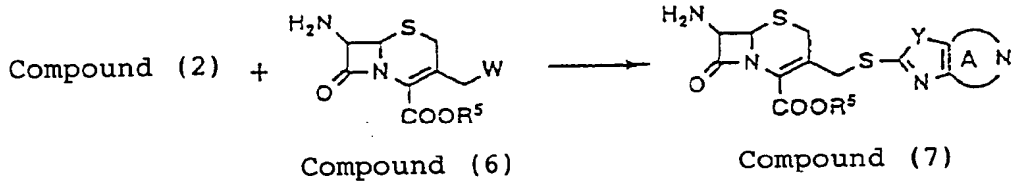
When R^3 is a trityl group, a formyl group or the like, R^4 is a trityl group, a tetrahydropyranyl group or the like and R^5 is p-methoxybenzyl group, diphenylmethyl group or the like, these groups can be deprotected under an acidic condition. In this instance, the compound (5) may be treated with a weak acid such as trifluoroacetic acid, formic acid or the like or a strong acid such as hydrochloric acid or the like. In the former case, the compound (5) is added to a weak acid which is used in an amount suitable for solvent use and allowed to react at 0 °C to room temperature for 1 to 2 hours. In the latter case, the compound (5) is reacted with 2 to 10 molar equivalents of a strong acid in methanol at 0 °C to room temperature for 1 to 2 hours.

When R^3 is an allyloxycarbonyl group or the like, R^4 is a trityl group or the like and R^5 is a p-nitrobenzyl group, a benzyl group, an allyl group or the like, part or all of these groups are eliminated under a reducing condition. In this instance, the compound (5) may be subjected to catalytic reduction using various types of catalyst, such as palladium-carbon, tetrakistriphenyl-phosphine palladium or the like or with a matallic reducing agent such as zinc or the like. The amount of the catalyst or the metallic reducing agent varies depending on the reactivity of the protective group. The reaction completes generally within 24 hours. Also, when R^3 is a chloroacetyl group, the compound (5) may be reacted with 1 to 2 molar equivalent various types of thioamide at 0 °C to room temperature for 1 to 2 hours. The thus obtained compound (I) can be crystallized and precipitated from its aqueous solution by adjusting pH. The compound (I) can be isolated and purified by means of a chromatography using a nonionic macroporous resin such as Diaion HP-20 or a gel filtration using Sephadex or the like.

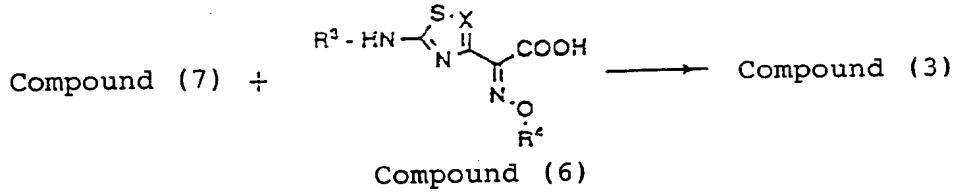
The cephalosporin derivatives represented by formula (I) according to the present invention can also be produced in accordance with a production process (B) which comprises steps (a) to (d), as diagrammatically shown below.

Production process (B)

Step a



Step b



Step c

Compound (3) + Compound (4) → Compound (5)

Step d

Compound (5) → Compound (I)

In the reaction scheme of the above steps (a) to (d), each of R^1, R^2, R^3, R^4, R^5, X, Y and W has the same meaning as described in the aforementioned production process (A).

In the step (a) of the above production process (B), a compound (6) and a compound (2) are allowed to react each other in the same manner as in the step 1 of the production process (A) to obtain a compound (7).

The starting compound (6) can be synthesized in accordance with the known method as described in the references quoted above for the synthesis of the compound (1).

In the step (b), a compound (3) is obtained by effecting acylation of the 7-position amino group of a 7-aminocephem compound (7) using a compound (8) which is an aminothiazolyl acetate derivative or an aminothiadiazolyl acetate derivative. The acylation reaction may be effected by a usually used means in the field of peptide synthesis chemistry. For example, the compound (3) may be obtained by allowing the 7-aminocephem compound (7) to react with an aminothiazolyl or aminothiadiazolyl acetate derivative (8) or an active derivative thereof in the presence of various types of condensing agent. Examples of the condensing agent include dicyclohexylcarbodiimide, vilsmeier reagent, phosphorous oxychloride and the like. These agents may be selected optionally depending on the reactivity and the like of the compound (7) and aminothiazolyl acetic acid or aminothiadiazolyl acetic acid (8) or an active derivative thereof. The molar ratio of the compound (8) and the condensing agent to the compound (7) both ranges from 1.1 to 1.5. Preferred examples of the reaction solvent include dichloromethane, chloroform, N,N-dimethylformamide, tetrahydrofuran and the like. The reaction may be carried out at a temperature in the range of from -20 to +50 °C, preferably from -20 to 0 °C for 1 to 2 hours. After completion of the reaction, the reaction mixture is subjected to usual after-treatments and, if necessary, the thus obtained compound (3) is purified by means of silica gel column chromatography and the like.

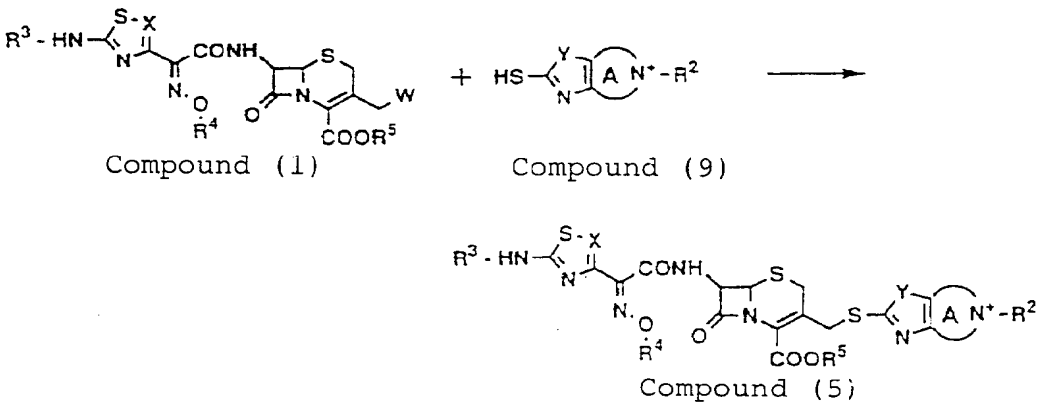
In the step (c), a compound (5) is obtained by allowing the compound (3) to react with a compound (4) in the same manner as in the step 2 of the aforementioned production process (A).

In the step (d), compound (I) is obtained by removing the protective group of compound (5) in the same manner as in the step 3 of the production process (A).

The cephalosporin derivatives represented by formula (I) according to the present invention can also be produced in accordance with a production process (C) which comprises steps i and ii, as diagrammatically shown below.

Production process (C)

Step i



Step ii

Compound (5) → Compound (I)

In the reaction scheme of the above steps i and ii, each of R^1, R^2, R^3, R^4, R^5, X, Y and W has the same meaning as described in the aforementioned production process (A).

In the step i of the above production process (C), a compound (1) and a compound (9) are allowed to react each other in the same manner as in the step 1 of the production process (A) to obtain a compound (5). The molar ratio of the compound (9) to the compound (1) ranges from 1.1 to 1.5.

In the step ii, the protective group of the compound (5) can be eliminated in the same manner as in the step 3 of the production process (A) to obtain the compound (I).

The thus obtained compound of formula (I) may be freeze-dried to be formulated into an antibacterial composition such as an injection upon use together with various pharmaceutically acceptable carriers such as fillers, binders and the like. The compound can be contained in the composition in an amount of 0.5 to 2 g, preferably 0.5 g, 1 g and 2 g per dosage form.

The cephalosporin derivatives of the present invention represented by formula (I) show strong antibacterial activities upon various pathogenic bacteria. The advantageous properties of typical examples of the compounds of the present invention are demonstrated in the following Test Example.

TEST EXAMPLE

Antibacterial activities of the following typical compounds A through E of the present invention represented by formula (I) upon various bacteria were determined by measuring the minimum inhibitory concentrations (MIC) in accordance with the known serial dilution technique. MIC was measured by inoculating 10^6 CFU/ml of each test strain on a Sensitivity Plate Medium N (Nissui Pharmaceutical Co., Ltd.), incubating the plates at 35 °C for 18 to 20 hours and then evaluating the results.

Test Compounds:

A: 7-{(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(5-methylthiazolo[4,5-c]pyridinium-2-yl)-thiomethyl-3-cephem-4-carboxylate

B: 7-{(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(4-methylthiazolo[4,5-b]pyridinium-2-yl)-thiomethyl-3-cephem-4-carboxylate

C: 7-{(Z)-2-(2-aminothiazol-4-yl)-2-carboxymethoxyiminoacetamido}-3-(5-methylthiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

D: 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido)-3-(5-methylthiazolo[4,5-c]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

E: 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(5-methylthiazolo[4,5-c]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Measured values of the minimum inhibitory concentration (μg/ml) of these compounds A to E are shown in Table 1.

Table 1

Test strain	Minimum Inhibitory Concentration (μg/ml) of the compounds:				
	A	B	C	D	E
S. aureus 209P JC-1	0.20	0.20	3.13	3.13	1.56
S. epidermidis ATCC14990	0.20	0.20	3.13	3.13	1.56
E. hirae ATCC8043	1.56	50	100	>100	>100
E. coli NIHJ JC-2	0.05	0.10	0.05	0.20	0.20
K. pneumoniae PCI602	0.05	0.05	<0.025	0.20	0.05
P. vulgaris GN76	0.39	0.20	<0.025	0.10	<0.025
M. morganii 1510/S-1	<0.025	0.10	<0.025	0.05	0.05
C. freundii GN346/16	0.10	0.10	0.20	0.39	0.39
E. cloacae G-0008	0.05	0.20	0.05	0.20	0.20
S. marcescens No.1	0.05	0.20	<0.025	0.05	0.05
P. aeruginosa E-2	50	25	12.5	3.13	1.56

As shown in Table 1, it can be found that the cephalosporin derivatives represented by formula (I) according to the present invention show strong antibacterial activities. Thus, the derivatives are expected to be useful as a drug for the treatment of infectious diseases caused by various pathogenic bacteria.

The following examples are provided to further illustrate the present invention, but are not to be construed to limit the scope of the invention.

EXAMPLE 1

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(thiazolo[4,5-c]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate

Five hundred mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl-)2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate was dissolved in 5 ml of acetone, 98 mg of sodium iodide was added thereto, and the resulting mixture was allowed to react at room temperature for 1 hour. After distilling off the solvent under a reduced pressure, 5 ml of N,N-dimethylformamide was added to the resulting residue to dissolve the residue therein and 116 mg of 2-mercaptothiazolo[4,5-c]pyridine was further added thereto. The resulting mixture was allowed to react at room temperature for 3.5 hours. To the reaction mixture were added 50 ml of ethyl acetate and 50 ml of 20% sodium chloride aqueous solution to separate an organic layer. The organic layer thus separated was washed with 20% sodium chloride aqueous solution and then dried over anhydrous magnesium sulfate. After distilling off the solvent under a reduced pressure, the resulting residue was purified by a column chromatography (70 g silica gel, toluene:ethyl acetate = 2:1) to obtain 443 mg of the title compound in a yield of 76%.

NMR ($CDCl_3$) δ, 3.62 (1 H, d, J = 18 Hz), 3.75 (1 H, d, J = 18 Hz), 3.79 (3 H, s), 4.05 (3 H, s), 4.27 (1 H, d, J = 13 Hz), 4.79 (1 H, d, J = 13 Hz), 5.01 (1 H, d, J = 5 Hz), 5.27 (2 H, s), 5.91 (1 H, dd, J = 5 Hz, 9 Hz), 6.72 (1 H, s), 6.80 (1 H, d, J = 9 Hz), 6.88 (2 H, d, J = 9 Hz), 7.00 (1 H, s), 7.15 - 7.30 (15 H, m), 7.36 (2 H, d, J = 9 Hz), 7.70 (1 H, d, J = 6 Hz), 8.45 (1 H, d, J = 6 Hz), 9.09 (1 H, s)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(5-methylthiazolo[4,5-c]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

A 443 mg portion of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(thiazolo[4,5-c]pyridine-2-yl)thiomethyl-3-cephem-4-carboxylate was dissolved in 4 ml of benzene and 3.0 ml of methyl iodide was added thereto to carry out the reaction at room temperature for 26 hours. After distilling off the solvent under a reduced pressure, 2.2 ml of anisole was added to the resulting residue and cooled on an ice bath. To this was added 4.4 ml of trifluoro acetate to carry out the reaction at the same temperature for 1 hour. Thereafter, the resulting reaction mixture was added dropwise to 22 ml of diisopropyl ether. The thus purified precipitate was collected, dried and then suspended in 3 ml of distilled water, and the suspension was adjusted to pH 7 with a saturated sodium hydrogencarbonate aqueous solution. The resulting suspension was charged on a column packed with 40 ml of Diaion HP-20 resin (Mitsubishi Kasei Corporation). The column was washed with water and then, elution was carried out using 5% acetone solution and 10% acetone solution in this order. After the fraction containing the desired compound was concentrated under reduced pressure, the residue was dissolved in water and freeze-dried to obtain 179 mg of the title compound in a yield of 65%.

NMR (D_2O) δ, 3.50 (1 H, d, J = 18 Hz), 3.90 (1 H, d, J = 18 Hz), 4.03 (3 H, s), 4.12 (1 H, d, J = 13 Hz), 4.52 (3 H, s), 5.07 (1 H, d, J = 13 Hz), 5.16 (1 H, d, J = 5 Hz), 5.80 (1 H, d, J = 5 Hz), 7.03 (1 H, s), 8.49 (1 H, d, J = 6 Hz), 8.55 (1 H, d, J = 6 Hz), 9.30 (1 H, s)

EXAMPLE 2

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(thiazolo[4,5-b]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 111 mg of 2-mercaptothiazolo[4,5-b]pyridine in place of 2-mercaptothiazolo[4,5-c]pyridine and 477 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate, the reaction and purification were carried out in the same manner as in Example 1 (a) to obtain 345 mg of the title compound in a yield of 62%.

NMR ($CDCl_3$) δ, 3.71 (1 H, d, J = 18 Hz), 3.80 (1 H, d, J = 18 Hz), 3.90 (3 H, s), 4.06 (3 H, s), 4.33 (1 H, d, J = 13 Hz), 4.86 (1 H, s, J = 13 Hz), 5.01 (1 H, d, J = 5 Hz), 5.26 (1 H, d, J = 6 Hz), 5.30 (1 H, d, J = 6 Hz), 5.90 (1 H, dd, J = 5 Hz, 9 Hz), 6.72 (1 H, s), 6.79 (1 H, d, J = 9 Hz), 6.89 (2 H, d, J = 9 Hz), 7.03 (1 H, s), 7.15 - 7.35 (16 H, m), 7.37 (2 H, d, J = 9 Hz), 8.10 (1 H, d, J = 6 Hz), 8.61 (1 H, d, J = 6 Hz)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(4-methylthiazolo[4,5-b]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 345 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(thiazolo[4,5-b]pyridine-2-yl)thiomethyl-3-cephem-4-carboxylate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 64 mg of the title compound in a yield of 46%.

NMR (D_2O) δ, 3.50 (1 H, d, J = 18 Hz), 3.85 (1 H, d, J = 18 Hz), 3.96 (3 H, s), 4.24 (1 H, d, J = 13 Hz), 4.53 (3 H, s), 4.99 (1 H, d, J = 13 Hz), 5.15 (1 H, d, J = 5 Hz), 5.77 (1 H, d, J = 5 Hz), 6.99 (1 H, s), 7.75 (1 H, t, J = 6 Hz), 8.68 (1 H, d, J = 6 Hz), 8.86 (1 H, d, J = 6 Hz)

EXAMPLE 3

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-diphenylmethoxycarbonylmethoxyiminoacetamido}-3-(thiazolo[4,5-c]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 402 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-diphenylmethoxycarbonylmethoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 74 mg of 2-mercaptothiazolo[4,5-c]pyridine, the reaction and purification were carried out in the same manner as in Example 1 (a) to obtain 356 mg of the title compound in a yield of 78%.

NMR ($CDCl_3$) δ, 3.37 (1 H, d, J = 18 Hz), 3.61 (1 H, d, J = 18 Hz), 3.79 (3 H, s), 4.22 (1 H, d, J =

13 Hz), 4.55 (1 H, d, J = 13 Hz), 4.94 (1 H, d, J = 5 Hz), 4.97 (1 H, d, J = 13 Hz), 5.00 (1 H, d, J = 13 Hz), 5.26 (1 H, d, J = 12 Hz), 5.30 (1 H, d, J = 12 Hz), 5.87 (1 H, dd, J = 5 Hz, 9 Hz), 6.77 (1 H, s), 6.87 (2 H, d, J = 9 Hz), 6.96 (1 H, s), 7.01 (1 H, s), 7.15 - 7.45 (27 H, m), 7.71 (1 H, d, J = 6 Hz), 7.98 (1 H, d, J = 9 Hz), 8.46 (1 H, d, J = 6 Hz), 9.10 (1 H, s)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-carboxymethoxyiminoacetamido}-3-(5-methylthiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 356 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl-)2-diphenylmethoxycarbonylmethoxyiminoacetamido}-3-(thiazolo[4,5-c]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 128 mg of the title compound as its sodium salt in a yield of 64%.

NMR (D_2O) δ, 3.47 (1 H, d, J = 18 Hz), 3.85 (1 H, d, J = 18 Hz), 4.02 (1 H, d, J = 13 Hz), 4.48 (3 H, s), 4.56 (2 H, s), 5.01 (1 H, d, J = 13 Hz), 5.12 (1 H, d, J = 5 Hz), 5.77 (1 H, d, J = 5 Hz), 7.01 (1 H, s), 8.45 (1 H, d, J = 6 Hz), 8.51 (1 H, d, J = 6 Hz), 9.27 (1 H, s)

EXAMPLE 4

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-(thiazolo[4,5-c]pyridin-2-yl)thiomethyl-3-cephem-4 carboxylate

Using 369 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-chloromethyl-3-cephem-4-carboxylate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 74 mg of 2-mercaptothiazolo[4,5-c]pyridine, the reaction and purification were carried out in the same manner as in Example 1 (a) to obtain 331 mg of the title compound in a yield of 79%.

NMR ($CDCl_3$) δ, 1.39 (9 H, s), 1.58 (3 H, s), 1.61 (3 H, s), 3.57 (1 H, d, J = 18 Hz), 3.74 (1 H, d, J = 18 Hz), 3.79 (3 H, s), 4.28 (1 H, d, J = 13 Hz), 4.80 (1 H, d, J = 13 Hz), 5.00 (1 H, d, J = 5 Hz), 5.23 (1 H, d, J = 12 Hz), 5.30 (1 H, d, J = 12 Hz), 5.97 (1 H, dd, J = 5 Hz, 9 Hz), 6.72 (1 H, s), 6.87 (2 H, d, J = 9 Hz), 7.15 - 7.40 (18 H, m), 7.70 (1 H, d, J = 6 Hz), 8.15 (1 H, d, J = 9 Hz), 8.46 (1 H, d, J = 6 Hz), 9.09 (1 H, s)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-(5-methylthiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 331 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-(thiazolo[4,5-c]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 138 mg of the title compound in the form of a sodium salt in a yield of 65%.

NMR (D_2O) δ, 1.48 (3 H, s), 1.50 (3 H, s), 3.48 (1 H, d, J = 18 Hz), 3.85 (1 H, d, J = 18 Hz), 4.10 (1 H, d, J = 13 Hz), 4.48 (3 H, s), 5.04 (1 H, d, J = 13 Hz), 5.13 (1 H, d, J = 5 Hz), 5.77 (1 H, d, J = 5 Hz), 6.96 (1 H, s), 8.46 (1 H, d, J = 6 Hz), 8.51 (1 H, d, J = 6 Hz), 9.27 (1 H, s)

EXAMPLE 5

(a) Preparation of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(thiazolo[4,5-c]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 306 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-chloromethyl-3-cephem-4-carboxylate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 56 mg of 2-mercaptothiazolo[4,5-c]pyridine, the reaction and purification were carried out in the same manner as in Example 1 (a) to obtain 276 mg of the title compound in a yield of 80%.

NMR ($CDCl_3$) δ, 1.57 (3 H, d, J = 7 Hz), 3.49 (1 H, d, J = 18 Hz), 3.65 (1 H, d, J = 18 Hz), 3.79 (3 H, s), 4.27 (1 H, d, J = 13 Hz), 4.84 (1 H, d, J = 13 Hz), 4.93 (1 H, d, J = 5 Hz), 5.16 (1 H, q, J = 7 Hz), 5.23 (1 H, d, J = 12 Hz), 5.31 (1 H, d, J = 12 Hz), 5.87 (1

H, dd, J = 5 Hz, 9 Hz), 6.73 (1 H, s), 6.86 (1 H, s), 6.90 (2 H, d, J = 9 Hz), 7.00 (1 H, s), 7.15 - 7.30 (25 H, m), 7.36 (2 H, d, J = 9 Hz), 7.70 (1 H, d, J = 6 Hz), 8.05 (1 H, d, J = 9 Hz), 8.45 (1 H, d, J = 6 Hz), 9.09 (1 H, s)

(b) Preparation of 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(5-methylthiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 276 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(thiazolo[4,5-c]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 84 mg of the title compound in the form of a sodium salt in a yield of 53%.

NMR (D_2O) δ, 1.46 (3 H, d, J = 7 Hz), 3.48 (1 H, d, J = 18 Hz), 3.85 (1 H, d, J = 18 Hz), 4.12 (1 H, d, J = 13 Hz), 4.49 (3 H, s), 4.65 (1 H, q, J = 7 Hz), 5.03 (1 H, d, J = 13 Hz), 5.14 (1 H, d, J = 5 Hz), 5.78 (1 H, d, J = 5 Hz), 6.99 (1 H, s), 8.46 (1 H, d, J = 6 Hz), 8.52 (1 H, d, J = 6 Hz), 9.28 (1 H, s)

EXAMPLE 6

Preparation of 7-{(Z)-2-(5-aminothiadiazol-3-yl)-2-methoxyiminoacetamido}-3-(5-methylthiazolo[4,5-c]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

A 141 mg portion of p-methoxybenzyl 7-{(Z)-2-(5-aminothiadiazol-3-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate was dissolved in 2 ml of N,N-dimethylformamide and 47 mg of sodium iodide and 70 mg of 2-mercapto-5-methylthiazolo[4,5-c]pyridinium chloride were added thereto to allow the mixture to react at room temperature for 3 hours. To the reaction mixture were added 50 ml of ethyl acetate and 50 ml of a 20% sodium chloride aqueous solution. The precipitate thus formed was collected by filtration and 1 ml of anisole was added thereto. After cooling on an ice bath, 2 ml of trifluoroacetate was added to the solution followed by reaction at the same temperature for 1 hour. The resulting reaction mixture was added dropwise to 10 ml of diisopropyl ether, the precipitate thus formed was collected by filtration, dried and suspended in 3 ml of distilled water. The resulting solution was adjusted to pH 7 with a saturated sodium hydrogencarbonate aqueous solution and treated with 15 ml of HP-20 resin for purification. The resulting solution was freeze-dried to obtain 46 mg of the title compound in a yield of 26%.

NMR (D_2O) δ, 3.46 (1H, d, J = 18 Hz), 3.88 (1H, d, J = 18 Hz), 4.07 (1H, d, J = 14 Hz), 4.08 (3H, s), 4.49 (3H, s), 5.07 (1H, d, J = 14 Hz), 5.12 (1H, d, J = 5 Hz), 5.80 (1H, d, J = 5 Hz), 8.47 (1H, d, J = 6 Hz)

EXAMPLE 7

Preparation of 7-{(Z)-2-(5-aminothiadiazol-3-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-(5-methylthiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 204 mg of p-methoxybenzyl 7-{(Z)-2-(5-aminothiadiazol-3-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-chloromethyl-3-cephem-4-carboxylate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 57 mg of 2-mercaptothiazolo[4,5-c]pyridine, the reaction and purification were carried out in the same manner as in Example 1 (a) and (b) to obtain 90 mg of the title compound in the form of a sodium salt in a yield of 45%.

NMR (D_2O) δ, 1.48 (6H, s), 3.43 (1H, d, J = 18 Hz), 3.82 (1H, d, J = 18 Hz), 4.07 (1H, d, J = 14 Hz), 4.43 (3H, s), 4.83 (1H, d, J = 14 Hz), 5.08 (1H, d, J = 5 Hz), 5.71 (1H, d, J = 5 Hz), 8.40 (1H, d, J = 6 Hz), 8.47 (1H, d, J = 6 Hz), 9.31 (1H, s)

EXAMPLE 8

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-diphenylmethoxycarbonylmethoxyiminoacetamido}-3-(thiazolo[4,5-b]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 301 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-diphenylmethoxycarbonylmethoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 60 mg of 2-mercaptothiazolo[4,5-b]-

pyridine in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercaptothiazolo[4,5-c]pyridine, respectively, the reaction and purification were carried out in the same manner as in Example 1 (a) to obtain 242 mg of the title compound in a yield of 71%.

NMR ($CDCl_3$) δ, 3.48 (1H, d, J = 18 Hz), 3.66 (1H, d, J = 18 Hz), 3.80 (3H, s), 4.29 (1H, d, J = 13 Hz), 4.85-5.05 (4H, m), 5.28 (1H, d, J = 12 Hz), 5.35 (1H, d, J = 12 Hz), 5.87 (1H, dd, J = 5 Hz, 9 Hz), 6.76 (1H, s), 6.88 (2H, d, J = 9 Hz), 6.95 (1H, s), 7.00 (1H, s), 7.15-7.45 (26H, m), 7.96 (1H, d, J = 9 Hz), 8.11 (1H, d, J = 7 Hz), 8.62 (1H, d, J = 7 Hz)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-carboxymethoxyiminoacetamide}-3-(4-methylthiazolo[4,5-b]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 242 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-diphenylmethoxycarbonylmethoxyiminoacetamido)-3-(thiazolo[4,5-b]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 33 mg of the title compound in the form of a sodium salt in a yield of 28%.

NMR (D_2O) δ, 3.51 (1H, d, J = 18 Hz), 3.85 (1 H, d, J = 18 Hz), 4.30 (1 H, d, J = 13 Hz), 4.53 (3H, s), 4.59 (2H, s), 4.95 (1H, d, J = 13 Hz), 5.19 (1 H, d, J = 5 Hz), 5.78 (1 H, d, J = 5 Hz), 6.94 (1 H, s), 7.76 (1 H, t, J = 7 Hz), 8.69 (1H, d, J = 7 Hz), 8.88 (1 H, d, J = 7 Hz)

EXAMPLE 9

Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-(thiazolo[4,5-b]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 276 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-chloromethyl-3-cephem-4-carboxylate and 60 mg of 2-mercaptothiazolo-[4,5-b]pyridine in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercaptothiazolo[4,5-c]pyridine, respectively, the reaction and purification were carried out in the same manner as in Example 1 (a) to obtain 191 mg of the title compound in a yield of 61%.

NMR ($CDCl_3$) δ, 1.40 (9H, s), 1.58 (3H, s), 1.62 (3H, s), 3.65 (1H, d, J = 18 Hz), 3.76 (1H, d, J = 18 Hz), 3.80 (3H, s), 4.35 (1H, d, J = 13 Hz), 4.89 (1H, d, J = 13 Hz), 5.00 (1H, d, J = 5 Hz), 5.25 (1H, d, J = 12 Hz), 5.35 (1H, d, J = 12 Hz), 5.97 (1H, dd, J = 5 Hz, 9 Hz), 6.70 (1H, s), 6.84-6.94 (3H, m), 7.20-7.46 (16 H, m), 8.10 (1H, d, J = 7 Hz), 8.18 (1H, d, J = 9 Hz), 8.61 (1H, d, J = 7 Hz)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-(4-methylthiazolo[4,5-b]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 191 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-(thiazolo[4,5-b]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 14 mg of the title compound in the form of a sodium salt in a yield of 11%.

NMR (D_2O) δ, 1.54 (3H, s), 1.56 (3H, s), 3.36 (1H, d, J = 18 Hz), 3.90 (1H, d, J = 18 Hz), 4.31 (1H, d, J = 13 Hz), 4.58 (3H, s), 5.03 (1H, d, J = 13 Hz), 5.21 (1H, d, J = 5 Hz), 5.83 (1H, d, J = 5 Hz), 7.02 (1H, s), 7.80 (1H, t, J = 7 Hz), 8.72 (1H, d, J = 7 Hz), 8.92 (1H, d, J = 7 Hz)

EXAMPLE 10

Preparation of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(thiazolo[4,5-b)pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 305 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-chloromethyl-3-cephem-4-carboxylate and 60 mg of 2-mercaptothiazolo[4,5-

b]pyridine in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercaptothiazolo[4,5-c]pyridine, respectively, the reaction and purification were carried out in the same manner as in Example 1 (a) to obtain 215 mg of the title compound in a yield of 62%.

NMR ($CDCl_3$) δ, 1.60 (3H, d, J = 7 Hz), 3.58 (1H, d, J = 18 Hz), 3.69 (1H, d, J = 18 Hz), 3.78 (3H, s), 4.33 (1H, d, J = 13 Hz), 4.90 (1H, J = 13 Hz), 4.92 (1H, d, J = 5 Hz), 5.16 (1H, q, J = 7 Hz), 5.25 (1H, d, J = 12 Hz), 5.35 (1H, d, J = 12 Hz), 5.88 (1H, dd, J = 5 Hz, 9 Hz), 6.71 (1H, s), 6.86 (2H, d, J = 9 Hz), 6.90 (1H, s), 6.99 (1H, s), 7.23-7.55 (28H, m), 8.00 (1H, d, J = 9 Hz), 8.08 (1H, d, J = 7 Hz), 8.61 (1H, d, J = 7 Hz)

(b) Preparation of 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxymethoxyimino}acetamido]-3-(4-methylthiazolo-[4,5-b]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 215 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(thiazolo[4,5-b]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 31 mg of the title compound in the form of a sodium salt in a yield of 72%.

NMR (D_2O) δ, 1.45 (3H, d, J = 7Hz), 3.53 (1H, d, J = 18 Hz), 3.85 (1H, d, J = 18 Hz), 4.30 (1H, d, J = 13 Hz), 4.55 (3H, s), 4.65 (1H, q, J = 7 Hz), 4.99 (1H, d, J = 13 Hz), 5.19 (1H, d, J = 5 Hz), 5.81 (1H, d, J = 5 Hz), 6.98 (1H, s), 7.77 (1H, t, J = 7 Hz), 8.70 (1H, d, J = 7 Hz), 8.89 (1H, d, J = 7Hz)

EXAMPLE 11

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido]-3-(thiazolo[5,4-c]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 60 mg of 2-mercaptothiazolo[5,4-c]pyridine in place of 2-mercaptothiazolo[4,5-c]pyridine and 238 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate, the reaction and purification were carried out in the same manner as in Example 1 (a) to obtain 186 mg of the title compound in a yield of 67%.

NMR ($CDCl_3$) δ, 3.59 (1H, d, J = 18 Hz), 3.75 (1H, d, J = 18 Hz), 3.80 (3H, s), 4.05 (3H, s), 4.26 (1H, d, J = 13 Hz), 4.82 (1H, d, J = 13 Hz), 5.02 (1H, d, J = 5 Hz), 5.26 (1H, d, J = 12 Hz), 5.30 (1H, d, J = 12 Hz), 5.92 (1H, dd, J = 5 Hz, 9 Hz), 6.72 (1H, s), 6.83 (1H, d, J = 9 Hz), 6.88 (2H, d, J = 9 Hz), 6.99 (1H, s), 7.10-7.55 (17H, m), 7.66 (1H, d, J = 7 Hz), 8.57 (1H, d, J = 7 Hz), 9.02 (1H, s)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(5-methylthiazolo[5,4-c]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 186 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(thiazolo[5,4-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 43 mg of the title compound in a yield of 51%.

NMR (D_2O) δ, 3.50 (1H, d, J = 18Hz), 3.89 (1H, d, J = 18 Hz), 4.01 (3H, s), 4.21 (1H, d, J = 13 Hz), 4.44 (3H, s), 5.05 (1H, d, J = 13 Hz), 5.18 (1H, d, J = 5 Hz), 5.80 (1H, d, J = 5 Hz), 7.03 (1H, s), 8.21 (1H, d, J = 7 Hz), 8.65 (1H, d, J = 7Hz), 9.34 (1H, s)

EXAMPLE 12

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-diphenylmethoxycarbonylmethoxyiminoacetamido}-3-(thiazolo[5,4-c]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 301 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-diphenylmethoxycarbonylmethoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 60 mg of 2-mercaptothiazolo[5,4-c]-pyridine in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercaptothiazolo[4,5-c]pyridine, respectively, the reaction and purification were carried out in the same manner as in Example 1 (a) to obtain 256 mg of the title

compound in a yield of 75%.

NMR ($CDCl_3$) δ, 3.34 (1H, d, J = 18 Hz), 3.60 (1H, d, J = 18 Hz), 3.78 (3H, s), 4.19 (1H, d, J = 13 Hz), 4.85-5.05 (4H, m), 5.24 (1H, d, J = 12 Hz), 5.33 (1H, d, J = 12 Hz), 5.87 (1H, dd, J = 5 Hz, 9 Hz), 6.76 (1H, s), 6.88 (2H, d, J = 9 Hz), 6.96 (1H, s), 7.00 (1H, s), 7.15-7.50 (27H, m), 7.65 (1H, d, J = 7 Hz), 7.98 (1H, d, J = 9 Hz), 8.56 (1H, d, J = 7 Hz), 9.02 (1H, s)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-carboxymethoxyiminoacetamido}-3-(5-methylthiazolo[5,4-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 256 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-diphenylmethoxycarbonylmethoxyiminoacetamido}-3-(thiazolo[5,4-c]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 59 mg of the title compound in the form of a sodium salt in a yield of 41%.

NMR (D_2O) δ, 3.50 (1H, d, J = 18Hz), 3.84 (1H, d, J = 18 Hz), 4.25 (1H, d, J = 13 Hz), 4.45 (3H, s), 4.59 (3H, s), 4.93 (1H, d, J = 13 Hz), 5.19 (1H, d, J = 5 Hz), 5.79 (1H, d, J = 5 Hz), 6.95 (1H, s), 8.18 (1H, d, J = 7Hz), 8.64 (1H, d, J = 7 Hz), 9.31 (1H, s)

EXAMPLE 13

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-(thiazolo[5,4-c]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 276 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-chloromethyl-3-cephem-4-carboxylate and 60 mg of 2-mercaptothiazolo-[5,4-c]pyridine in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyimino-acetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercaptothiazolo[4,5-c]pyridine, respectively, the reaction and purification were carried out in the same manner as in Example 1 (a) to obtain 215 mg of the title compound in a yield of 68%.

NMR ($CDCl_3$) δ, 1.40 (9H, s), 1.58 (3H, s), 1.62 (3H, s), 3.54 (1H, d, J = 18 Hz), 3.71 (1H, d, J = 18 Hz), 3.79 (3H, s), 4.25 (1H, d, J = 13 Hz), 4.84 (1H, d, J = 13 Hz), 5.00 (1H, d, J = 5 Hz), 5.24 (1H, d, J = 12 Hz), 5.33 (1H, d, J = 12 Hz), 5.97 (1H, dd, J = 5 Hz, 9 Hz), 6.72 (1H, s), 6.85-6.95 (3H, m), 7.10-7.40 (17H, m), 7.66 (1H, d, J = 7 Hz), 8.02 (1H, d, J = 9 Hz), 8.56 (1H, d, J = 7 Hz), 9.01 (1H, s)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-(5-methylthiazolo-[5,4-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 215 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-(thiazolo[5,4-c]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 69 mg of the title compound in the form of a sodium salt in a yield of 51%.

NMR (D_2O) δ, 1.50 (3H, s), 1.52 (3H, s), 3.50 (1H, d, J = 18 Hz), 3.85 (1H, d, J = 18 Hz), 4.25 (1H, d, J = 13 Hz), 4.43 (3H, s), 4.97 (1H, d, J = 13 Hz), 5.18 (1H, d, J = 5 Hz), 5.80 (1H, d, J = 5 Hz), 6.93 (1H, s), 8.19 (1H, d, J = 7Hz), 8.64 (1H, d, J = 7 Hz), 9.31 (1H, s)

EXAMPLE 14

(a) Preparation of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(thiazolo[5,4-c]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 305 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-chloromethyl-3-cephem-4-carboxylate and 60 mg of 2-mercaptothiazolo[5,4-c]pyridine in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercaptothiazolo[4,5-c]pyridine, respectively, the reaction and purification were carried out in the same manner as in Example 1 (a) to obtain 218 mg of the title compound in a yield of 63%.

NMR ($CDCl_3$) δ, 1.60 (1H, d, J = 7 Hz), 3.47 (1H, d, J = 18 Hz), 3.65 (1H, d, J = 18 Hz), 3.79 (3H,

s), 4.25 (1H, d, J = 13 Hz), 4.88 (1H, d, J = 13 Hz), 4.93 (1H, d, J = 5 Hz), 5.18 (1H, q, J = 7 Hz), 5.23 (1H, d, J = 12 Hz), 5.34 (1H, d, J = 12 Hz), 5.87 (1H, dd, J = 5 Hz, 9 Hz), 6.73 (1H, s), 6.80-6.95 (3H, m), 6.98 (1H, s), 7.10-7.40 (27H, m), 7.65 (1H, d, J = 7 Hz), 8.05 (1H, d, J = 9 Hz), 8.57 (1H, d, J = 7 Hz), 9.01 (1H, s)

(b) Preparation of 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(5-methylthiazolo-[5,4-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 218 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(thiazolo[5,4-c]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 62 mg of the title compound in the form of a sodium salt in a yield of 49%.

NMR (D_2O) δ, 1.47 (3H, d, J = 7 Hz), 3.49 (1H, d, J = 18 Hz), 3.84 (1H, d, J = 18 Hz), 4.25 (1H, d, J = 13 Hz), 4.43 (3H, s), 4.68 (1H, q, J = 7 Hz), 4.94 (1H, d, J = 13 Hz), 5.19 (1H, d, J = 5 Hz), 5.79 (1H, d, J = 5 Hz), 6.93 (1H, s), 8.18 (1H, d, J = 7Hz), 8.63 (1H, d, J = 7 Hz), 9.31 (1H, s)

EXAMPLE 15

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(4-methylthiazolo-[5,4-b]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate

A 238 mg portion of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate was dissolved in 3 ml of acetone, 47 mg of sodium iodide was added thereto and the resulting mixture was allowed to react at room temperature for 1 hour. After the solvent was distilled off under a reduced pressure, 3 ml of N,N-dimethylformamide was added to dissolve the residue. A 107 mg portion of 2-mercapto-4-methylthiazolo[5,4-b]pyridinium trifluoroacetate was added thereto followed by reaction at room temperature for 3 hours. To the reaction mixture were added 50 ml of dichloromethane and 50 ml of a 20% sodium chloride aqueous solution for separation of an organic layer. The organic layer was washed with a 20% sodium chloride aqueous solution and a 5% sodium thiosulfate aqueous solution and dried over anhydrous magnesium sulfate. After the solvent was distilled off under a reduced pressure, the residue was subjected to gel column chromatography LH-20 (chloroform : methanol = 1 : 1) for purification to obtain 227 mg of the title compound in a yield of 72%.

NMR ($CDCl_3$) δ, 3.52 (1H, d, J = 18 Hz), 3.77 (1H, d, J = 18 Hz), 3.80 (3H, s), 4.05 (3H, s), 4.27 (1H, d, J = 13 Hz), 4.77 (3H, s), 4.86 (1H, d, J = 13 Hz), 5.07 (1H, d, J = 5 Hz), 5.21 (1H, d, J = 12 Hz), 5.33 (1H, d, J = 12 Hz), 5.90 (1H, dd, J = 5 Hz, 9 Hz), 6.67 (1H, s), 6.82 (1H, d, J = 9 Hz), 6.88 (2H, d, J = 9 Hz), 7.05 (1H, s), 7.20-7.30 (15H, m), 7.36 (2H, d, J = 9 Hz), 8.97 (1H, dd, J = 7 Hz, 9 Hz), 8.37 (1H, d, J = 9 Hz), 9.74 (1H, d, J = 7 Hz)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-methoxyimino}acetamido]-3-(4-methylthiazolo[5,4-b]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 227 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido]-3-(4-methylthiazolo[5,4-b]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 65 mg of the title compound in a yield of 52%.

NMR (D_2O) δ, 3.49 (1H, d, J = 18 Hz), 3.89 (1H, d, J = 18 Hz), 3.99 (3H, s), 4.14 (1H, d, J = 13 Hz), 4.51 (3H, s), 5.02 (1H, d, J = 13 Hz), 5.14 (1H, d, J = 5 Hz), 5.77 (1H, d, J = 5 Hz), 7.00 (1H, s), 8.02 (1H, dd, J = 7Hz, 9 Hz), 8.77 (2H, d, J = 7 Hz)

EXAMPLE 16

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-diphenylmethoxycarbonylmethoxyiminoacetamido}-3-(4-methylthiazolo-[5,4-b]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 301 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-diphenylmethoxycarbonylmethoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 107 mg of 2-mercapto-4-methylthiazolo-[5,4-b]pyridinium trifluoroacetate, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 305 mg of the title compound in a yield of 80%.

NMR ($CDCl_3$) δ, 3.28 (1H, d, J = 18 Hz), 3.64 (1H, d, J = 18 Hz), 3.79 (3H, s), 4.16 (1H, d, J = 13 Hz), 4.67 (3H, s), 4.85-5.05 (4H, m) 5.21 (1H, d, J = 12 Hz), 5.36 (1H, d, J = 12 Hz), 5.83 (1H, dd, J = 5 Hz, 9 Hz), 6.76 (1H, s), 6.89 (2H, d, J = 9 Hz), 6.95 (1H, s), 7.20-7.40 (28H, m), 7.91 (1H, dd, J = 7 Hz, 9 Hz), 8.03 (1H, d, J = 9 Hz), 8.30 (1H, d, J = 9 Hz), 9.42 (1H, d, J = 7 Hz)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-carboxymethoxyiminoacetamido}-3-(4-methylthiazolo-[5,4-b]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 305 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-diphenylmethoxycarbonylmethoxyiminoacetamido}-3-(4-methylthiazolo[5,4-b]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 105 mg of the title compound in a yield of 68%.

NMR (D_2O) δ, 3.49 (1H, d, J = 18 Hz), 3.86 (1H, d, J = 18 Hz), 4.16 (1H, d, J = 13 Hz), 4.50 (3H, s), 4.56 (2H s), 4.99 (1H, d, J = 13 Hz), 5.14 (1H, d, J = 5 Hz), 5.79 (1H, d, J = 5 Hz), 7.03 (1H, s), 8.01 (1H, t, J = 9 Hz), 8.76 (2H, d, J = 9 Hz)

EXAMPLE 17

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-(4-methylthiazolo-[5,4-b]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 277 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-chloromethyl-3-cephem-4-carboxylate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 107 mg of 2-mercapto-4-methylthiazolo-[5,4-b]pyridinium trifluoroacetate, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 327 mg of the title compound in a yield of 92%.

NMR ($CDCl_3$) δ, 1,41 (9H, s), 1.58 (3H, s), 1.62 (3H, s), 3.45 (1H, d, J = 18 Hz), 3.76 (1H, d, J = 18 Hz), 3.79 (3H, s), 4.22 (1H, d, J = 13 Hz), 4.76 (3H, s), 4.91 (1H, d, J = 13 Hz), 5.07 (1H, d, J = 5 Hz), 5.20 (1H, d, J = 12 Hz), 5.35 (1H, d, J = 12 Hz), 5.94 (1H, dd, J = 5 Hz, 9 Hz), 6.70 (1H, s), 6.80-6.90 (3H, m), 7.20-7.30 (15H, m), 7.36 (2H, d, J = 9 Hz), 7.98 (1H, dd, J = 7 Hz, 9 Hz), 8.17 (1H, d, J = 9 Hz), 8.36 (1H, d, 9 Hz), 9.45 (1H, d, J = 7 Hz)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-(4-methylthiazolo-[5,4-b]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 327 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-(4-methylthiazolo[5,4-b]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 128 mg of the title compound in the form of a sodium salt in a yield of 69%.

NMR (D_2O) δ, 1.49 (3H, s), 1.50 (3H, s), 3.50 (1H, d, J = 18 Hz), 3.87 (1H, d, J = 18 Hz), 4.16 (1H, d, J = 13 Hz), 4.51 (3H, s), 5.00 (1H, d, J = 13 Hz), 5.15 (1H, d, J = 5 Hz), 5.79 (1H, d, J = 5 Hz), 6.98 (1H, s), 8.02 (1H, t, J = 9 Hz), 8.77 (2H, d, J = 9 Hz)

EXAMPLE 18

(a) Preparation of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(4-methylthiazolo-[5,4-b]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 306 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-chloromethyl-3-cephem-4-carboxylate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 107 mg of 2-mercapto-4-methylthiazolo-[5,4-b]pyridinium trifluoroacetate, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 329 mg of the title compound in a yield of 86%.

NMR ($CDCl_3$) δ, 1.60 (3H, d, J = 7 Hz), 3.40 (1H, d, J = 18 Hz), 3.70 (1H, d, J = 18 Hz), 3.78 (3H, s), 4.18 (1H, d, J = 13 Hz), 4.68 (3H, s), 5.01 (1H, d, J = 5 Hz), 5.16 (1H, q, J = 7 Hz), 5.19 (1H, d, J = 12 Hz), 5.35 (1H, d, J = 12 Hz), 5.85 (1H, dd, J = 5 Hz, 9 Hz), 6.71 (1H, s), 6.87 (2H d, J = 9 Hz), 6.90 (1H, s), 6.98 (1H, s), 7.15-7.35 (25H, m), 7.36 (2H, d, J = 9 Hz), 7.96 (1H, dd, J = 7 Hz, 9 Hz), 8.02 (1H d, J = 9 Hz), 8,33 (1H, d, J = 9 Hz), 9.47 (1H, d, J = 7 Hz)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(4-methylthiazolo-[5,4-b]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 329 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(4-methylthiazolo[5,4-b]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 108 mg of the title compound in the form of a sodium salt in a yield of 64%.

NMR (D_2O) δ, 1.45 (3H, d, J = 7 Hz), 3.49 (1H, d, J = 18 Hz), 3.86 (1H, d, J = 18 Hz), 4.15 (1H, d, J = 13 Hz), 4.50 (3H, s), 4.65 (1H, q, J = 7 Hz), 4.99 (1H, d, J = 13 Hz), 5.14 (1H, t, J = 5 Hz), 5.79 (1H, d, J = 5 Hz), 7.01 (1H, s), 8.01 (1H, dd, J = 7 Hz, 9 Hz), 8.76 (1H, d, J = 7 Hz), 8.76 (1H, d, J = 9Hz)

EXAMPLE 19

(a) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(5-carboxymethylthiazolo-[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

A 312 mg portion of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(thiazolo[4,5-c]pyridin-2-yl)thiomethyl-3-cephem-4-carboxylate was dissolved in 3 ml of benzene, 815 mg of tert-butyl iodoacetate was added thereto and the resulting mixture was allowed to react at room temperature for 51 hours. After the solvent was distilled off under a reduced pressure, the residue was dissolved in water and charged on a column packed with Sephadex LH-20 (Pharmacia). Elution was carried out with 50% methanol solution. Then, 1.5 ml of anisole was added to the fraction containing the desired compound followed by cooling on an ice bath. After further adding 3.0 ml of trifluoroacetate thereto, the resulting mixture was allowed to react at the same temperature for 30 minutes and then at room temperature for 3 hours. The reaction mixture was added dropwise to 15 ml of diisopropyl ether. The precipitate thus formed was collected by filtration, dried and suspended in 3 ml of distilled water. The resulting solution was adjusted to pH 7 with a saturated sodium hydrogencarbonate aqueous solution and treated with 30 ml of Diaion HP-20 resin for purification followed by freeze-drying to obtain 95 mg of the title compound in the form of a sodium salt in a yield of 44%.

NMR (D_2O) δ, 3.49 (1H, d, J = 18 Hz), 3.86 (1H, d, J = 18 Hz), 3.98 (1H, s), 4.15 (1H, d, J = 13 Hz), 4.96 (1H, d, J = 13 Hz), 5.14 (1H, d, J = 5 Hz), 5.32 (2H, s), 5.78 (1H, d, J = 5 Hz), 7.00 (1H, s), 8.51 (2H, s), 9.26 (1H, s)

EXAMPLE 20

(a) Preparation of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(5-methylthiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 306 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-chloromethyl-3-cephem-4-carboxylate and 112 mg of 5-ethyl-2-mercaptothiazolo[4,5-c]pyridinium trifluoroacetate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercapto-4-methylthiazolo-[5,4-b]pyridinium trifluoroacetate, respectively, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 322 mg of the title compound in a yield of 83%.

NMR ($CDCl_3$) δ, 1.60 (3H, d, J = 7 Hz), 1.72 (3H, d, J = 7 Hz), 3.42 (1H, d, J = 18 Hz), 3.68 (1H, d, J = 18 Hz), 3.78 (3H, s), 4.22 (1H, d, J = 13 Hz), 4.89 (1H, d, J = 13 Hz), 4.90-5.05 (3H, m), 5.17 (1H, d, J = 7 Hz), 5.23 (1H, d, J = 13 Hz), 5.35 (1H, d, J = 13 Hz), 5.87 (1H, dd, J = 5 Hz, 9 Hz), 6.72 (1H, s), 6.87 (2H, d, J = 9 Hz), 6.91 (1H, s), 6.98 (1H, br-s), 7.20-7.35 (20H, m), 7.36 (2H, d, J = 9 Hz), 8.06 (1H, d, J = 9 Hz), 8.69 (1H, d, J = 7 Hz), 9.15 (1H, s), 9.33 (1H, d, J = 7 Hz)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(5-ethylthiazolo-[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 322 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(5-ethylthiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 112 mg of the title compound in the form of a sodium salt in a yield of 67%.

NMR (D_2O) δ, 1.45 (3H, d, J = 7 Hz), 1.68 (3H, t, J = 7 Hz), 3.47 (1H, d, J = 18 Hz), 3.85 (1H, d, J = 18 Hz), 4.11 (1H, d, J = 13 Hz), 4.64 (1H, q, J = 7 Hz), 4.74 (2H, q, J = 7 Hz), 5.04 (1H, d, J = 13 Hz), 5.13 (1H, d, J = 5 Hz), 5.79 (1H, d, J = 5 Hz), 7.00 (1H, s), 8.48 (1H, d, J = 7 Hz), 8.59 (1H, d, J = 7 Hz), 9.35 (1H, s)

EXAMPLE 21

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-(5-methylthiazolo-[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 277 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-chloromethyl-3-cephem-4-carboxylate and 112 mg of 5-ethyl-2-mercaptothiazolo-[4,5-c]pyridinium trifluoroacetate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercapto-4-methylthiazolo[5,4-b]-pyridinium trifluoroacetate, respectively, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 253 mg of the title compound in a yield of 70%.

NMR ($CDCl_3$) δ, 1.41 (9H, s), 1.58 (3H, s), 1.61 (3H, s), 1.72 (3H, d, J = 7 Hz), 3.46 (1H, d, J = 18 Hz), 3.76 (1H, d, J = 18 Hz), 3.78 (3H, s), 4.21 (1H, d, J = 13 Hz), 4.90 (1H, d, J = 13 Hz), 4.95 (2H, q, J = 7 Hz), 5.02 (1H, d, J = 5 Hz), 5.23 (1H, d, J = 12 Hz), 5.35 (1H, d, J = 12 Hz), 5.96 (1H, dd, J = 5 Hz, 9 Hz), 6.72 (1H, s), 6.87 (2H, d, J = 9 Hz), 7.20-7.35 (15H, m), 7.37 (2H, d, J = 9 Hz), 8.18 (1H, d, J = 9 Hz), 8.73 (1H, d, J = 9 Hz), 9.12 (1H, s), 9.28 (1H, d, J = 9 Hz)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-(5-ethylthiazolo-[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 253 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-(5-ethylthiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 92 mg of the title compound in the form of a sodium salt in a yield of 64%.

NMR (D_2O) δ, 1.48 (3H, s), 1.49 (3H, s), 1.69 (3H, t, J = 7 Hz), 3.48 (1H, d, J = 18 Hz), 3.85 (1H, d, J = 18 Hz), 4.12 (1H, d, J = 13 Hz), 4.74 (2H, q, J = 7 Hz), 5.03 (1H, d, J = 13 Hz), 5.13 (1H, d, J = 5 Hz), 5.77 (1H, d, J = 5 Hz), 6.96 (1H, s), 8.48 (1H, d, J = 6 Hz), 8.60 (1H, d, J = 6 Hz), 9.35 (1H, s)

EXAMPLE 22

(a) Preparation of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-{5-(2-fluoroethyl)thiazolo-[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 306 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-chloromethyl-3-cephem-4-carboxylate and 118 mg of 5-(2-fluoroethyl)-2-

mercaptothiazolo-[4,5-c]pyridinium trifluoroacetate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercapto-4-methylthiazolo-[5,4-b]pyridinium trifluoroacetate, respectively, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 280 mg of the title compound in a yield of 71%.

NMR ($CDCl_3$) δ, 1.61 (3H, d, J = 7 Hz), 3.43 (1H, d, J = 18 Hz), 3.67 (1H, d, J = 18 Hz), 3.78 (3H, s), 4.27 (1H, d, J = 13 Hz), 4.85 (1H, d, J = 13 Hz), 4.95 (1H, d, J = 5 Hz), 4.98 (2H, dt, J = 4 Hz, 47 Hz), 5.10-5.45 (5H, m), 5.88 (1H, dd, J = 5 Hz, 9 Hz), 6.72 (1H, s), 6.87 (2H, d, J = 9 Hz), 6.90 (1H, s), 6.97 (1H, s), 7.20-7.35 (25H, m), 7.35 (2H, d, J = 9 Hz), 8.03 (1H, d, J = 9 Hz), 8.46 (1H, d, J = 7 Hz), 9.11 (1H, d, J = 7 Hz), 9.24 (1H, s)

(b) Preparation of 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-{5-(2-fluoroethyl)-thiazolo-[4,5-c]pyridinium-2-yl}thiomethyl-3-cephem-4-carboxylate

Using 280 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-{5-(2-fluoroethyl)thiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 102 mg of the title compound in the form of a sodium salt in a yield of 69%.

NMR (D_2O) δ, 1.46 (1H, d, J = 7 Hz), 3.48 (1H, d, J = 18 Hz), 3.86 (1H, d, J = 18 Hz), 4.12 (1H, d, J = 13 Hz), 4.65 (1H, q, J = 7 Hz), 4.90-5.15 (6H, m), 5.79 (1H, d, J = 5 Hz), 7.01 (1H, s), 8.53 (1H, d, J = 7 Hz), 8.62 (1H, d, J = 7 Hz), 9.38 (1H, s)

EXAMPLE 23

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-{5-(2-fluoroethyl)thiazolo[4,5-c]pyridinium-2-yl}thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 277 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-chloromethyl-3-cephem-4-carboxylate and 118 mg of 5-(2-fluoroethyl)-2-mercaptothiazolo[4,5-c]pyridinium trifluoroacetate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercapto-4-methylthiazolo-[5,4-b]pyridinium trifluoroacetate, respectively, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 271 mg of the title compound in a yield of 74%.

NMR ($CDCl_3$) δ, 1.41 (9H, s), 1.62 (3H, s), 1.64 (3H, s), 3.47 (1H, d, J = 18 Hz), 3.73 (1H, d, J = 18 Hz), 3.79 (3H, s), 4.29 (1H, d, J = 13 Hz), 4.83 (1H, d, J = 13 Hz), 4.90-5.40 (7H, m), 5.97 (1H, dd, J = 5 Hz, 9 Hz), 6.71 (1H, s), 6.85-6.90 (3H, m), 7.25-7.40 (17H, m), 8.17 (1H, d, J = 9 Hz), 8.51 (1H, d, J = 6 Hz), 9.19 (1H, d, J = 6 Hz), 9.27 (1H, s)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-{5-(2-fluoroethyl)thiazolo[4,5-c]pyridinium-2-yl}thiomethyl-3-cephem-4-carboxylate

Using 271 mg of p-methoxybenzyl 7-{(Z)-2(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-{5-(2-fluoroethyl)thiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 107 mg of the title compound in the form of a sodium salt in a yield of 68%.

NMR (D_2O) δ, 1.48 (3H, s), 1.50 (3H, s), 3.47 (1H, d, J = 18 Hz), 3.86 (1H, d, J = 18 Hz), 4.12 (1H, d, J = 13 Hz), 4.90-5.20 (6H, m), 5.78 (1H, d, J = 5 Hz), 6.98 (1H, s), 8.53 (1H, d, J = 6 Hz), 8.62 (1H, d, J = 6 Hz), 9.38 (1H, s)

EXAMPLE 24

(a) Preparation of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(5-(2-hydroxyethyl)thiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 306 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-chloromethyl-3-cephem-4-carboxylate and 117 mg of 5-(2-hydroxyethyl)-2-mercaptothiazolo[4,5-c]pyridinium trifluoroacetate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercapto-4-methylthiazolo-[5,4-b]pyridinium trifluoroacetate, respectively, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 314 mg of the title compound in a yield of 80%.

NMR ($CDCl_3$) δ, 1.60 (3H, d, J = 7 Hz), 3.42 (1H, d, J = 18 Hz), 3.69 (1H, d, J = 18 Hz), 3.77 (3H, s), 4.00-4.10 (2H, m), 4,22 (1H, d, J = 13 Hz), 4.80-4.95 (3H, m), 4.97 (1H, d, J = 5 Hz), 5.16 (1H, q, J = 7 Hz), 5.22 (1H, d, J = 12 Hz), 5.33 (1H, d, J = 12 Hz), 5.87 (1H, dd, J = 5 Hz, 9 Hz), 6.72 (1H, s), 6.86 (2H, d, J = 9 Hz), 6.89 (1H, s), 6.97 (1H, s), 7.20-7.35 (25H, m), 7.36 (2H, d, J = 9 Hz), 8.02 (1H, d, J = 9 Hz), 8.43 (1H, d, J = 6 Hz), 8.92 (1H, d, J = 6 Hz), 9.18 (1H, s)

(b) Preparation of 7-[(Z)-2-(2-aminothiaxol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-{5-(2-hydroxyethyl)thiazolo[4,5-c]pyridinium-2-yl}thiomethyl-3-cephem-4-carboxylate

Using 314 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-{5-(2-hydroxyethyl)thiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 119 mg of the title compound in the form of a sodium salt in a yield of 72%.

NMR (D_2O δ, 1.46 (3H, d, J = 7 Hz), 3.48 (1H, d, J = 18 Hz), 3.86 (1H, d, J = 18 Hz), 4.05-4.20 (3H, m), 4.65 (1H, q, J = 7 Hz), 4.80-4.90 (2H, m), 5.05 (1H, d, J = 13 Hz), 5.14 (1H, d, J = 5 Hz), 5.79 (1H, d, J = 5 Hz), 7.02 (1H, s), 8.51 (1H, d, J = 7 Hz), 8.60 (1H, d, J = 7 Hz), 9.34 (1H, s)

EXAMPLE 25

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyiminoacetamido}-3-{5-(2-hydroxyethyl)thiazolo[4,5-c]pyridinium-2-yl}thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 277 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-chloromethyl-3-cephem-4-carboxylate and 117 mg of 5-(2-hydroxyethyl)-2-mercaptothiazolo[4,5-c]pyridinium trifluoroacetate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercapto-4-methylthiazolo-[5,4-b]pyridinium trifluoroacetate, respectively, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 313 mg of the title compound in a yield of 86%.

NMR ($CDCl_3$) δ, 1.41 (9H, s), 1.58 (3H, s), 1.60 (3H, s), 3.47 (1H, d, J = 18 Hz), 3.76 (1H, d, J = 18 Hz), 3.79 (3H, s), 4.05-4.15 (2H, m), 4.24 (1H, d, J = 13 Hz), 4.85 (1H, d, J = 13 Hz), 4.90-5.00 (2H, m), 5.04 (1H, d, J = 5 Hz), 5.23 (1H, d, J = 12 Hz), 5.34 (1H, d, J = 12 Hz), 5.94 (1H, dd, J = 5 Hz, 9 Hz), 6.71 (1H, s), 6.87 (2H, d, J = 9 Hz), 6.88 (1H, s), 7.20-7.35 (15H, m), 7.37 (2H, d, J = 9 Hz), 8.19 (1H, d, J = 9 Hz), 8.45 (1H, d, J = 6 Hz), 8.96 (1H, d, J = 6 Hz), 9.17 (1H, s)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-{5-(2-hydroxyethyl)thiazolo[4,5-c]pyridinium-2-yl}thiomethyl-3-cephem-4-carboxylate

Using 313 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-{5-(2-hydroxyethyl)thiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 101 mg of the title compound in the form of a sodium salt in a yield of 56%.

NMR (D_2O) δ, 1.49 (3H, s), 1.50 (3H, s), 3.47 (1H, d, J = 18 Hz), 3.87 (1H, d, J = 18 Hz), 4.05-4.15 (3H, m), 4.85-4.95 (2H, m), 5.06 (1H, d, J = 13 Hz), 5.14 (1H, d, J = 5 Hz), 5.78 (1H, d, J = 5 Hz), 6.98 (1H, s), 8.52 (1H, d, J = 6 Hz), 8.60 (1H, d, J = 6 Hz), 9.35 (1H, s)

EXAMPLE 26

(a) Preparation of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(5-carbamoylmethylthiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 306 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-chloromethyl-3-cephem-4-carboxylate and 117 mg of 5-carbamoylmethyl-2-mercaptothiazolo[4,5-c]pyridinium trifluoroacetate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercapto-4-methylthiazolo-[5,4-b]pyridinium trifluoroacetate, respectively, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 229 mg of the title compound in a yield of 58%.

NMR ($CDCl_3$) δ, 1.61 (3H, d, J = 7 Hz), 3.41 (1H, d, J = 18 Hz), 3.65 (1H, d, J = 18 Hz), 3.77 (3H, s), 4.29 (1H, d, J = 13 Hz), 4.77 (1H, d, J = 13 Hz), 4.95 (1H, d, J = 5 Hz), 5.15 (1H, q, J = 7 Hz), 5.22 (1H, d, J = 12 Hz), 5.31 (1H, d, J = 12 Hz), 5.85-6.20 (4H, m), 6.71 (1H, s), 6.85 (2H, d, J = 9 Hz), 6.89 (1H, s), 7.00 (1H, s), 7.20-7.30 (25H, m), 7.34 (2H d, J = 9 Hz), 8.07 (1H, d, J = 9 Hz), 8.34 (1H, d, J = 7 Hz), 9.00-9.15 (2H, m), 9.40 (1H, s)

(b) Preparation of 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(5-carbamoylmethylthiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 229 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(5-carbamoylmethylthiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 82 mg of the title compound in the form of a sodium salt in a yield of 68%.

NMR (D_2O) δ, 1.46 (3H, d, J = 7 Hz), 3.48 (1H, d, J = 18 Hz), 3.86 (1H, d, J = 18 Hz), 4.12 (1H, d, J = 13 Hz), 4.65 (1H, q, J = 7 Hz), 5.06 (1H, d, J = 13 Hz), 5.13 (1H, d, J = 5 Hz), 5.60 (2H, s), 5.79 (1H d, J = 5 Hz), 7.01 (1H, s), 8.54 (2H, s), 9.30 (1H, s)

EXAMPLE 27

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-(5-carbamoylmethylthiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 277 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-chloromethyl-3-cephem-4-carboxylate and 153 mg of 5-carbamoylmethyl-2-mercaptothiazolo-[4,5-c]pyridinium trifluoroacetate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercapto-4-methylthiazolo[5,4-b]pyridinium trifluoroacetate, respectively, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 223 mg of the title compound in a yield of 61%.

NMR ($CDCl_3$) δ, 1.39 (9H, s), 1.58 (3H, s), 1.59 (3H, s), 3.44 (1H, d, J = 18 Hz), 3.73 (1H, d, J = 18 Hz), 3.76 (3H, s), 4.28 (1H, d, J = 13 Hz), 4.75 (1H, d, J = 13 Hz), 5.01 (1H, d, J = 5 Hz), 5.21 (1H, d, J = 12 Hz), 5.30 (1H, d, J = 12 Hz), 5.90-6.00 (3H, m), 6.40 (1H, m), 6.70 (1H, s), 6.84 (2H, d, J = 9 Hz), 6.94 (1H, s), 7.20-7.40 (17H, m), 8.15 (1H, d, J = 9 Hz), 8.42 (1H, m), 8.95 (1H, m), 9.10 (1H, m), 9.40 (1H, s)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-(1-carboxy-1-methylethoxyimino)acetamido}-3-(5-carbamoylmethylthiazolo[4,5-c]pyridinium-2-yl}thiomethyl-3-cephem-4-carboxylate

Using 223 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-(1-tert-butoxycarbonyl-1-methylethoxyimino)acetamido}-3-(5-carbamoylthiazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 89 mg of the title compound in the form of a sodium salt in a yield of 68%.

NMR (D_2O) δ, 1.48 (3H, s), 1.50 (3H, s), 3.48 (1H, d, J = 18 Hz), 3.86 (1H, d, J = 18 Hz), 4.12 (1H,

d, J = 13 Hz), 5.06 (1H, d, J = 13 Hz), 5.13 (1H, d, J = 5 Hz), 5.60 (2H, s), 5.78 (1H, d, J = 5 Hz), 6.98 (1H, s), 8.54 (2H, s), 9.31 (1H, s)

EXAMPLE 28

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(5-methyloxazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 100 mg of 2-mercapto-5-methyloxazolo[4,5-c]pyridinium trifluoroacetate in place of 2-mercapto-4-methylthiazolo[5,4-b]pyridiniumtrifluoroacetate and 235 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 261 mg of the title compound in a yield of 85%.

NMR ($CDCl_3$) δ, 3.51 (1H, d, J = 18 Hz), 3.79 (1H, d, J = 18 Hz), 4.30 (1H, d, J = 13 Hz), 4.76 (3H, s), 4.88 (1H, d, J = 13 Hz), 5.03 (1H, d, J = 5 Hz), 5.21 (1H, d, J = 12 Hz), 5.33 (1H, d, J = 12 Hz), 5.88 (1H, dd, J = 5 Hz, 9 Hz), 6.73 (1H, s), 7.10-7.40 (15H, m), 8.03 (1H, d, J = 9 Hz), 9.15 (1H, s), 9.32 (1H, d, J = 9 Hz)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(5-methyloxazolo[4,5-c]-pyridinium-2-yl}thiomethyl-3-cephem-4-carboxylate

Using 261 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-(5-methyloxazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 63 mg of the title compound in a yield of 45%.

NMR (D_2O) δ, 3.51 (1H, d, J = 18 Hz), 3.93 (1H, d, J = 18 Hz), 4.02 (3H, s), 4.14 (1H, d, J = 13 Hz), 4.50 (3H, s), 4.95 (1H, d, J = 13 Hz), 5.17 (1H, d, J = 5 Hz), 5.82 (1H, d, J = 5 Hz), 7.03 (1H, s), 8.15 (1H, d, J = 6 Hz), 8.72 (1H, d, J = 6 Hz), 9.19 (1H, s)

EXAMPLE 29

(a) Preparation of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-diphenylmethoxycarbonylmethoxyiminoacetamido}-3-(5-methyloxazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 300 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-diphenylmethoxycarbonylmethoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 100 mg of 2-mercapto-5-methyloxazolo[4,5-c]pyridinium trifluoroacetate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercapto-4-methylthiazolo[5,4-b]pyridinium trifluoroacetate, respectively, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 302 mg of the title compound in a yield of 81%.

NMR ($CDCl_3$) δ, 3.43 (1H, d, J = 18 Hz), 3.66 (1H, d, J = 18 Hz), 3.78 (3H, s), 4.02 (2H, s), 4.30 (1H, d, J = 13 Hz), 4.75 (1H, d, J = 13 Hz), 4.96 (1H, d, J = 5 Hz), 5.22 (1H, d, J = 12 Hz), 5.34 (1H, d, J = 12 Hz), 5.85 (1H, dd, J = 5 Hz, 9 HZ), 6.77 (1H, s), 7.10-7.40 (15H, m), 8.05 (1H, d, J = 9 Hz), 9.16 (1H, s), 9.35 (1H, d, J = 9 Hz)

(b) Preparation of 7-{(Z)-2-(2-aminothiazol-4-yl)-2-carboxymethoxyiminoacetamido}-3-(5-methyloxazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 302 mg of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-diphenylcarbonylmethoxyiminoacetamido}-3-(5-methyloxazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 88 mg of the title compound in the form of a sodium salt in a yield of 58%.

NMR (D_2O) δ, 3.75 (1H, d, J = 18 Hz), 4.12 (1H, d, J = 18 Hz), 4.38 (1H, d, J = 12 Hz), 4.72 (3H, s), 4.84 (2H, s), 5.13 (1H, d, J = 12 Hz), 5.41 (1H, d, J = 5 Hz), 6.05 (1H, d, J = 5 Hz), 7.29 (1H, s), 8.39 (1H, d, J = 6 Hz), 8.96 (1H, d, J = 6 Hz), 9.42 (1H, s)

EXAMPLE 30

(a) Preparation of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(5-methyloxazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 303 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-chloromethyl-3-cephem-4-carboxylate and 100 mg of 2-mercapto-5-methyloxazolo[4,5-c]pyridinium trifluoroacetate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercapto-4-methylthiazolo-[5,4-b]pyridinium trifluoroacetate, respectively, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 331 mg of the title compound in a yield of 88%.

NMR ($CDCl_3$) δ, 1.58 (3H, d, J = 7 Hz), 3.42 (1H, d, J = 18 Hz), 3.63 (1H, d, J = 18 Hz), 3.78 (3H, s), 4.29 (1H, d, J = 13 Hz), 4.78 (1H, d, J = 13 Hz), 4.98 (1H, d, J = 5 Hz), 5.14 (1H, q, J = 7 Hz), 5.25 (1H, d, J = 12 Hz), 5.33 (1H, d, J = 12 Hz), 5.82 (1H, dd, J = 5 Hz, 9 Hz), 6.72 (1H, s), 7.10-7.40 (15H, m), 8.05 (1H, d, J = 9 Hz), 9.17 (1H, s), 9.35 (1H, d, J = 9 Hz)

(b) Preparation of 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(5-methyloxazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 331 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(5-methyloxazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 98 mg of the title compound in the form of a sodium salt in a yield of 58%.

NMR (D_2O) δ, 1.46 (3H, d, J = 7 Hz), 3.49 (1H, d, J = 18 Hz), 3.88 (1H, d, J = 14 Hz), 4.47 (3H, s), 4.66 (1H, q, J = 7 Hz), 5.17 (1H, d, J = 5 Hz), 5.79 (1H, d, J = 5 Hz), 6.97 (1H, s), 8.12 (1H, d, J = 6 Hz), 8.69 (1H, d, J = 6 Hz), 9.15 (1H, s)

EXAMPLE 31

Preparation of 7-{(Z)-2-(5-aminothiadiazol-3-yl)-2-methoxyiminoacetamido}-3-(5-methyloxazolo[4,5-c]-pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 100 mg of 2-mercapto-5-methyloxazolo[4,5-c]pyridinium trifluoroacetate in place of 2-mercapto-5-methylthiazolo[4,5-c]pyridiniumchloride and 163 mg of p-methoxybenzyl 7-{(Z)-2-(5-aminothiadiazol-3-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate, the reaction and purification were carried out in the same manner as in Example 6 to obtain 62 mg of the title compound in the form of a sodium salt in a yield of 31%.

NMR (D_2O) δ, 3.48 (1H, d, J = 18 Hz), 3.90 (1H, d, J = 18 Hz), 4.01 (1H, d, J = 14 Hz), 4.08 (3H, d), 4.93 (1H, d, J = 14 Hz), 5.13 (1H, d, J = 5 Hz), 5.82 (1H, d, J = 5 Hz), 8.13 (1H, d, J = 6 Hz), 8.71 (1H, d, J = 6 Hz), 9.17 (1H, s)

EXAMPLE 32

(a) Preparation of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(5-methylthiazolo[4,5-d]pyridazinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 170 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-chloromethyl-3-cephem-4-carboxylate and 60 mg of 2-mercapto-5-methylthiazolo[4,5-d]pyridazinium trifluoroacetate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercapto-4-methylthiazolo-[5,4-b]pyridinium trifluoroacetate, respectively, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 198 mg of the title compound in a yield of 93%.

NMR ($CDCl_3$) δ, 1.60 (3H, d, J = 7 Hz), 3.45 (1H, d, J = 18 Hz), 3.76 (1H, d, J = 18 Hz), 3.79 (3H, s), 4.25 (1H, d, J = 13 Hz), 4.65 (3H, s), 4.94 (1H, d, J = 5 Hz), 5.03 (1H, d, J = 13 Hz), 5.10-5.40 (3H, m), 5.85 (1H, dd, J = 5 Hz, 9 Hz), 6.72 (1H, s), 6.80-7.45 (31H,

m), 8.00 (1H, d, J = 9 Hz), 9.92 (1H, s), 10.17 (1H, s)

(b) Preparation of 7-[(Z)-2-(2-aminothiazol-4-yl)-2{(S)-1-carboxyethoxyimino}acetamido]-3-(5-methylthiazolo-[4,5-d]pyridazinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 198 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(5-methylthiazolo[4,5-d]pyridazinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 26 mg of the title compound in the form of a sodium salt in a yield of 25%.

NMR (D_2O) δ, 1.49 (3H, d, J = 7 Hz), 3.49 (1H, d, J = 18 Hz), 3.87 (1H, d, J = 18 Hz), 4.20 (1H, d, J = 13 Hz), 4.68 (1H, d, J = 13 Hz), 4.71 (3H, s), 5.16 (1H, d, J = 5 Hz), 5.81 (1H, d, J = 5 Hz), 7.04 (1H, s), 9.83 (1H, s), 10.03 (1H, s)

EXAMPLE 33

(a) Preparation of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(5,5-dimethyl-4H,6H,7H-thiazolo[5,4-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 306 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-chloromethyl-3-cephem-4-carboxylate and 113 mg of 5,5-methyl-2-mercapto-4H,6H,7H-thiazolo[4,5-c]pyridinium trifluoroacetate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercapto-4-methylthiazolo[5,4-b]pyridinium trifluoroacetate, respectively, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 242 mg of the title compound in a yield of 62%.

NMR ($CDCl_3$) δ, 1.60 (3H, d, J = 7 Hz), 3.10 (2H, m), 3.37 (1H, d, J = 18 Hz), 3.50-3.60 (7H, m), 3.81 (3H, m), 3.90-4.05 (2H, m), 4.06 (1H, d, J = 13 Hz), 4.49 (1H, d, J = 13 Hz), 4.95-5.00 (3H, m), 5.14 (1H, d, J = 12 Hz), 5.17 (1H, q, J = 7 Hz), 5.25 (1H, d, J = 12 Hz), 5.85 (1H, dd, J = 5 Hz, 9 Hz), 6.73 (1H, s), 6.89 (1H, s), 6.90 (2H, d, J = 9 Hz), 6.98 (1H, s), 7.20-7.40 (27H, m), 8.00 (1H, d, J = 9 Hz)

(b) Preparation of 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(5,5-dimethyl-4H,6H,7H-thiazolo[5,4-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

Using 242 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(5,5-dimethyl-4H,6H,7H-thiazolo[5,4-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 79 mg of the title compound in the form of a sodium salt in a yield of 63%.

NMR (D_2O) δ, 1.46 (3H, d, J = 7 Hz), 3.20-3.30 (8H, m), 3.41 (1H, d, J = 18 Hz), 3.75-3.90 (4H, m), 4.57 (1H, d, J = 13 Hz), 4.65 (1H, q, J = 7 Hz), 4.73 (2H, s), 5.18 (1H, d, J = 5 Hz), 5.77 (1H, d, J = 5 Hz), 7.04 (1H, s)

EXAMPLE 34

(a) Preparation of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(1,5-dimethylimidazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate trifluoroacetate

Using 306 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-chloromethyl-3-cephem-4-carboxylate and 153 mg of 1,5-dimethyl-2-mercaptoimidazolo[4,5-c]pyridinium trifluoroacetate in place of p-methoxybenzyl 7-{(Z)-2-(2-tritylaminothiazol-4-yl)-2-methoxyiminoacetamido}-3-chloromethyl-3-cephem-4-carboxylate and 2-mercapto-4-methylthiazolo[5,4-b]pyridinium trifluoroacetate, respectively, the reaction and purification were carried out in the same manner as in Example 15 (a) to obtain 334 mg of the title compound in a yield of 88%.

NMR ($CDCl_3$) δ, 1.60 (3H, d, J = 7 Hz), 3.46 (1H, d, J = 18 Hz), 3.71 (1H, d, J = 18 Hz), 3.79 (3H, s), 3.85 (3H, s), 4.20 (1H, d, J = 13 Hz), 4.50 (3H, s), 4.87 (1H, d, J = 13 Hz), 4.97

(1H, d, J = 5 Hz), 5.16 (1H, q, J = 7 Hz), 5.20 (1H, d, J = 12 Hz), 5.39 (1H, d, J = 13 Hz), 5.86 (1H, dd, J = 5 Hz, 9 Hz), 6.72 (1H, s), 6.89 (2H, d, J = 9 Hz), 6.90 (1H, s), 6.98 (1H, s), 7.20-7.35 (25H, m), 7.39 (2H, d, J = 9 Hz), 8.03 (1H, d, J = 9 Hz), 8.21 (1H, d, J = 6 Hz), 8.51 (1H, s), 8.99 (1H, d, J = 6 Hz)

(b) Preparation of 7-[(Z)-2-(2-aminothiazol-4-yl)-2-{(S)-1-carboxyethoxyimino}acetamido]-3-(1,5-dimethylimidazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylate

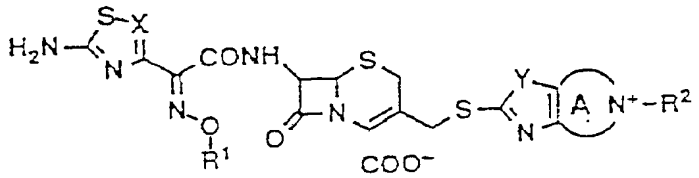
Using 334 mg of p-methoxybenzyl 7-[(Z)-2-(2-tritylaminothiazol-4-yl)-2-{(S)-1-diphenylmethoxycarbonylethoxyimino}acetamido]-3-(1,5-dimethylimidazolo[4,5-c]pyridinium-2-yl)thiomethyl-3-cephem-4-carboxylatetrifluoroacetate as a starting material, the reaction and purification were carried out in the same manner as in Example 1 (b) to obtain 87 mg of the title compound in the form of a sodium salt in a yield of 51%.

NMR (D_2O) δ, 1.45 (3H, d, J = 7 Hz), 3.49 (1H, d, J = 18 Hz), 3.83 (1H, d, J = 18 Hz), 3.86 (3H, s), 4.18 (1H, d, J = 13 Hz), 4.40 (3H, s), 4.65 (1H, q, J = 7 Hz), 4.69 (1H, d, J = 13 Hz), 5.16 (1H, d, J = 5 Hz), 5.78 (1H, d, J = 5 Hz), 6.99 (1H, s), 7.91 (1H, d, J = 7 Hz), 8.41 (1H, d, J = 7 Hz), 8.99 (1H, s)

While the invention has been described in detail and with reference to specific examples thereof, it will be apparent to one skilled in the art that various changes and modifications can be made therein without departing from the spirit and scope thereof.

Claims

1. A cephalosporin derivative represented by formula (I):



(I)

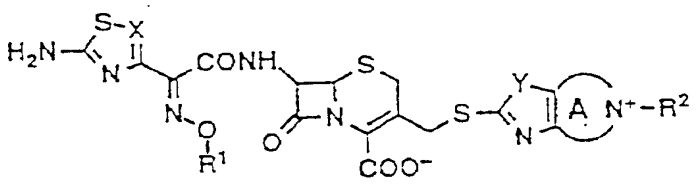
wherein X is a carbon atom or a nitrogen atom; Y is a sulfur atom, an oxygen atom or a nitrogen atom substituted with a substituted or unsubstituted lower alkyl group; R^1 is a hydrogen atom, a lower alkyl group or a substituted lower alkyl group; R^2 is a lower alkyl group, a substituted lower alkyl group, a lower alkylene group or a substituted lower alkylene group; and A is an unsaturated six-membered heterocyclic ring containing at least one nitrogen atom, or a pharmaceutically acceptable salt thereof.

2. The cephalosporin derivative according to claim 1, wherein the lower alkyl and alkylene groups have 1 to 4 carbon atoms.

3. The cephalosporin derivative according to claim 1, wherein the substituted lower alkyl and alkylene groups are the alkyl and alkylene groups each substituted with a substituent selected from the group consisting of a halogen atom, a hydroxyl group, a carboxyl group, a carbamoyl group, an amino group, an alkylamino group having 1 to 4 carbon atoms and these substituents substituted with an alkyl group having 1 to 4 carbon atoms, an alkylene group having 1 to 4 carbon atoms or an aralkyl group having 7 to 10 carbon atoms.

4. The cephalosporin derivative according to claim 1, wherein A is the heterocyclic ring selected from the group consisting of pyridine, pyrimidine, pyrazine, pyridazine, their dihydro or tetrahydro derivatives, thiazine, thiadiazine, oxazine and oxadiazine.

5. An antibacterial composition which comprises a cephalosporin derivative represented by formula (I)::



(I)

wherein X is a carbon atom or a nitrogen atom; Y is a sulfur atom, an oxygen atom or a substituted or unsubstituted lower alkyl group; R^1 is a hydrogen atom, a lower alkyl group or a substituted lower alkyl group; R^2 is a lower alkyl group, a substituted lower alkyl group, a lower alkylene group or a substituted lower alkylene group; and A is an unsaturated six-membered heterocyclic ring containing at least one nitrogen atom, or a pharmaceutically acceptable salt thereof as an active ingredient, and a pharmaceutically acceptable carrier.

6. The antibacterial composition according to claim 5, wherein the lower alkyl and alkylene groups have 1 to 4 carbon atoms.

7. The antibacterial composition according to claim 5, wherein the substituted lower alkyl and alkylene groups are the alkyl and alkylene groups each substituted with a substituent selected from the group consisting of a halogen atom, a hydroxyl group, a carboxyl group, a carbamoyl group, an amino group, an alkylamino group having 1 to 4 carbon atoms and these substituents substituted with an alkyl group having 1 to 4 carbon atoms, an alkylene group having 1 to 4 carbon atoms or an aralkyl group having 6 to 10 carbon atoms.

8. The antibacterial composition according to claim 5, wherein A is the heterocyclic ring selected from the group consisting of pyridine, pyrimidine, pyrazine, pyridazine, their dihydro or tetraphydro derivatives, thiazine, thiadiazine, oxazine and oxadiazine.

9. The use of the cephalosporin derivative according to claim 1 for the preparation of the antibacterial composition.

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 93 12 0533

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.5)
A	EP-A-0 248 645 (TANABE SEIYAKU CO., LTD.) * examples 22,23,67 *	1-9	C07D501/36 A61K31/545
A	DATABASE WPI Week 8751, Derwent Publications Ltd., London, GB; AN 87-359771 & JP-A-62 263 184 (OTSUKA KAGAKU YAKUHIN) * abstract * & CAS REGISTRY HANDBOOK 1988 SUPPL. (STN DATABASE) * RN: 115861-93-3, 115861-92-2 *	1-9	
A	EP-A-0 229 369 (TAKEDA CHEMICAL INDUSTRIES, LTD.) * examples 1,7 *	1-9	
A	EP-A-0 225 634 (TAKEDA CHEMICAL INDUSTRIES, LTD.) * examples 1,2 *	1-9	
A	DATABASE WPI Week 7614, Derwent Publications Ltd., London, GB; AN 76-25204 & JP-A-51 019 790 (FUJISAWA PHARM. IND. KK.) * abstract * & CAS REGISTRY HANDBOOK 1976 SUPPL. (STN DATABASE) * RN: 59943-85-0, 59943-82-7 *	1-9	TECHNICAL FIELDS SEARCHED (Int.Cl.5) C07D A61K

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
BERLIN	22 March 1994	Frelon, D

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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A : technological background
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T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
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EPO FORM 1503 03.82 (P04C01)

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 0 706 795 A2

(12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
17.04.1996 Bulletin 1996/16

(21) Application number: **95306159.5**

(22) Date of filing: **04.09.1995**

(51) Int Cl.[6]: **A61K 31/44**, A61K 31/515, A61K 31/235, A61K 31/445, A61K 31/165, A61K 31/415, A61K 31/11, A61K 31/12, A61K 31/055

(84) Designated Contracting States:
AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE

(30) Priority: **21.09.1994 US 310171**

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(54) Catechol diether compounds as inhibitors of TNF release

(57) This invention relates to the use of catechol diether compounds for the manufacture of a medicament for use as an inhibitor of tumor necrosis factor (TNF). The catechol diether compounds are useful as inhibitors of TNP per se and in the treatment or alleviation of inflammatory conditionsor disease, including but not limited to rheumatoid arthritis, osteoarthritis, asthma, bronchitis, chronic obstructive airways disease, psoriasis, allergic rhinitis, dermatitis and inflammatory bowel disease, sepsis, septic shock, tubercolosis, graft versus host disease and cachexis associated with AIDS or cancer.

EP 0 706 795 A2

Description

Background of the Invention

This invention relates to a method of inhibiting production of TNF (tumor necrosis factor) in a mammal in need thereof which method comprises administering to said mammal an effective amount of a compound of the formula (I) (shown below) or a pharmaceutically acceptable salt thereof, which, as such are also useful in the treatment or alleviation of inflammatory conditions or disease, including but not limited to rheumatoid arthritis, osteoarthritis, asthma, bronchitis, chronic obstructive airways disease, psoriasis, allergic rhinitis, dermatitis and inflammatory bowel disease, sepsis, septic shock, tuberculosis, multiple sclerosis and other autoimmune diseases, graft versus host disease and cachexia associated with AIDS or cancer; and this invention also relates to pharmaceutical compositions useful therefor.

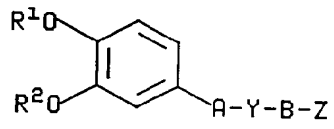
TNF is produced by monocytes/macrophages and has a variety of biological activities relevant to the pathogenesis of rheumatoid arthritis (RA) and osteoarthritis (OA). Firstly, TNF can promote the accumulation of all leukocyte types by stimulating the endothelium to express adhesion molecules (T.H. Pohlman et al., *J. Immunol.*, 136, pp. 4548-4553, 1986) and to release secondary chemotactic cytokines such as interleukin 8 (R.M. Strieter et al., *Science*, 243. pp. 1467-1469, 1989). Secondly, TNF can stimulate cells within the joint to synthesize and express the inducible cyclooxygenase enzyme (COX 2) and the inducible NO synthase. The products of these enzymes, prostaglandins and NO, are important mediators of pain and inflammation. Thirdly, and perhaps most importantly, TNF, like IL-1, can activate chondrocytes to degrade their own extracellular matrix and suppress synthesis of cartilage matrix components leading to cartilage destruction. In addition to these effects, TNF plays a pivotal role in the regulation of the production of other cytokines. This has been demonstrated in cultures of dissociated RA synovial cells where blocking the activity of TNF can inhibit the secretion of IL-1 (F.M. Brennan et al., *Lancet*, 2, pp. 244-247, 1989). Thus, blocking TNF production should prevent the synthesis of other downstream cytokines such as IL-1. Finally, TNF has been immunolocalised in both RA and OA synovial membranes (M.N. Farahat et al., *Ann. Rheum. Dis.*, 52, pp. 870-875, 1993).

TNF is recognized to be involved in many infectious and auto-immune diseases (W. Fiers, FEBS *Letters,* 1991, 285, p. 199). Furthermore, it has been shown that TNF is the prime mediator of the inflammatory response seen in sepsis and septic shock (C.E. Spooner et al., *Clinical Immunology and Immunopathology*, 1992, 62, p. S11).

The compounds utilized in the present invention are disclosed and claimed in WO-A-94/12461 wherein said compounds are disclosed as having phosphodiesterase type IV (PDE_{IV}) inhibiting activity. The teachings thereof are incorporated herein by reference.

Summary of the Invention

This invention is concerned with a method of inhibiting production of tumor necrosis factor (TNF) in a mammal in need thereof and/or a method of treating or alleviating inflammatory conditions or disease, including but not limited to rheumatoid arthritis, osteoarthritis, asthma, bronchitis, chronic obstructive airways disease, psoriasis, allergic rhinitis, dermatitis and inflammatory bowel disease, sepsis, septic shock, tuberculosis, multiple sclerosis and other autoimmune diseases, graft versus host disease and cachexia associated with AIDS or cancer which method comprises administering to said mammal an effective amount of a compound selected from the group consisting of compounds of the formula (I)



,

(I)

the racemic-diastereomeric mixtures and optical isomers of said compounds and the pharmaceutically acceptable salts thereof wherein

R^1 is selected from the group consisting of methyl, ethyl, difluoromethyl and trifluoromethyl;

R^2 is selected from the group consisting of (C_1-C_6)alkyl, alkoxyalkyl having 3 to 7 carbons in the alkoxy portion and 2 to 4 carbons in the alkyl portion, phenoxyalkyl having 2 to 6 carbons in the alkyl portion, (C_3-C_7)cycloalkyl, (C_6-C_9) polycycloalkyl, phenylalkyl having 1 to 8 carbons in the alkyl portion, phenylaminoalkyl having 2 to 6 carbons in the alkyl portion and the amino may be optionally substituted with (C_1-C_4) alkyl and indanyl,

where the alkyl portion of said alkyl, phenoxyalkyl, cycloalkyl, polycycloalkyl, phenylalkyl and indanyl may optionally be substituted with one or more fluorine atoms, -OH or (C_1-C_4)alkoxy,

and the aryl portion of said phenylalkyl, phenoxyalkyl and indanyl may optionally be substituted with (C_1-C_4)alkyl,

$(C_1\text{-}C_4)$alkoxy or halogen;

A and B are independently selected from the group consisting of a covalent bond, optionally substituted $(C_1\text{-}C_5)$alkylene, optionally substituted $(C_2\text{-}C_5)$alkenyl and optionally substituted phenylene,

where said optionally substituted alkylene may be monosubstituted and each substituent is selected from the group consisting of oxo, $(C_1\text{-}C_4)$alkoxy, CO_2R^6 and hydroxy,

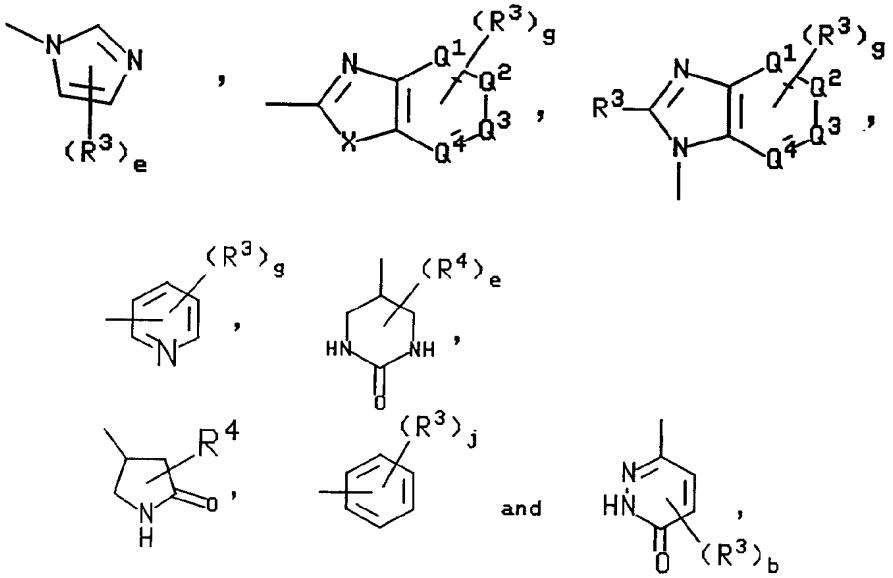
said optionally substituted alkenyl may be monosubstituted with $(C_1\text{-}C_4)$alkoxy or CO_2R^6, and

said optionally substituted phenylene may be monosubstituted with $(C_1\text{-}C_4)$alkoxy, CO_2R^6 or hydroxy,

wherein R^6 is hydrogen or $(C_1\text{-}C_4)$alkyl;

Y is selected from the group consisting of a covalent bond, O, NR^6 and S wherein R^6 is as defined above;

Z is selected from the group consisting of



where Q^1, Q^2, Q^3, and Q^4 are independently N, CH or, when also bonded to B, C and provided that at least two of Q^1, Q^2, Q^3, and Q^4 are not N;

X is selected from the group consisting of NR^4 and S;

e is an integer from 1 to 3;

g is an integer from 1 to 4;

j is an integer from 1 to 5;

each R^3 is independently selected from the group consisting of hydrogen, halogen, CF_3, $(C_1\text{-}C_6)$alkyl, $CH(R^7)CO_2R^4$, $(C_1\text{-}C_6)$alkoxy, CO_2R^4, $CONR^4R^5$, CONHOH, $CH_2NR^4R^5$, NR^4R^5, nitro, hydroxy, CN, SO_3H, phenylalkyl having 1 to 4 carbons in the alkyl portion, $SO_2NR^4R^5$, $N(SO_2R^8)_2$ and $NHSO_2R^8$,

where R^4 for each occurrence is independently selected from the group consisting of hydrogen, $(C_1\text{-}C_6)$alkyl, phenyl optionally substituted with $(C_1\text{-}C_4)$alkyl or halogen, $CH(R^7)CO_2R^6$, $(C_3\text{-}C_7)$cycloalkyl, phenylalkyl having 1 to 4 carbons in the alkyl portion and dialkylaminoalkyl having a total of 5 carbons in the dialkylamino portion and having 2 to 5 carbons in the alkyl portion where R^6 is as defined above,

R^5 for each occurrence is independently selected from the group consisting of hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_7)$ cycloalkyl, phenylalkyl having 1 to 4 carbons in the alkyl portion, phenyl, pyridyl, pyrimidyl, thiazolyl and oxazolyl,

or R^4 and R^5 are taken together with the nitrogen to which they are attached and form an optionally substituted saturated or unsaturated 5- or 6-membered ring, a saturated or unsaturated 6-membered heterocyclic ring containing two heteroatoms, or a quinoline ring optionally substituted with fluoro,

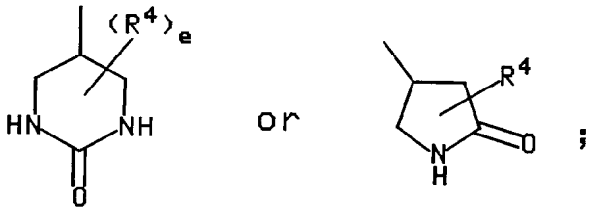
where said optionally substituted saturated or unsaturated 5- or 6-membered ring may be mono- or di-substituted and each substituent is independently selected from the group consisting of alkyl having 1 to 4 carbons, CO_2R^7 wherein R^7 is as defined below, $CONH_2$, $CON(CH_3)_2$, oxo, hydroxy, NH_2 and $N(CH_3)_2$, and said saturated or unsaturated 6-membered heterocyclic ring containing two heteroatoms has the second heteroatom selected from the group consisting of O, S, NH, NCH_3, $NCOCH_3$ and NCH_2Ph;

R^7 for each occurrence is independently selected from the group consisting of hydrogen and $(C_1\text{-}C_4)$alkyl;

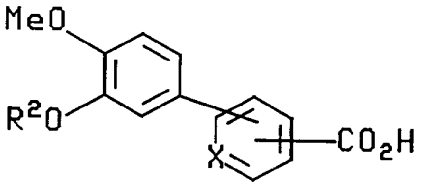
and R^8 is selected from the group consisting of $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_7)$cycloalkyl, phenyl and phenylalkyl having 1 to 4 carbons in the alkyl portion;

with the proviso that:

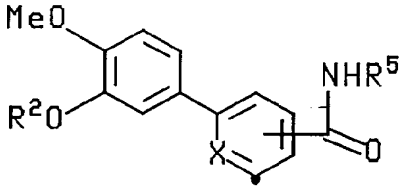
when R^1 is methyl or ethyl; R^2 is $(C_7\text{-}C_9)$polycycloalkyl or indanyl; A, B and Y are covalent bonds; X is N; and R^3 is hydrogen;
then Z is not



when the compound of formula I is



wherein X is CH or N and R^2 is as defined above for formula 1, the CO_2H can only be in the para position relative to the bond to the catechol moiety;
when the compound of formula I is



wherein X is CH or N and R^2 and R^5 are as defined above for formula I, the amide can only be in the para or meta position; and the compound of formula I cannot be *trans*-1-[4-[2-[3-(cyclopentyloxy)-4-methoxy-phenyl]-ethenylphenyl]-2-methyl-1H-imidazo[4,5c]-pyridine.

This invention is further directed to a method of treating or alleviating inflammatory conditions or disease, sepsis, septic shock, tuberculosis, multiple sclerosis and other autoimmune diseases, graft versus host disease or cachexia associated with AIDS or cancer in a mammal in need thereof which method comprises administering to said mammal an effective amount of a compound selected from the group consisting of compounds of the formula (I) as defined hereinabove. Thus in a further aspect, this invention provides a method of treating or alleviating rheumatoid arthritis, osteoarthritis, asthma, bronchitis, chronic obstructive airways disease, psoriasis, allergic rhinitis, dermatitis or inflammatory bowel disease, in a mammal in need thereof which comprises administering to said mammal an effective amount of a compound selected from the group consisting of compounds of the formula (I) as defined hereinabove.

Further still, this invention provides pharmaceutical compositions comprising a pharmaceutically acceptable diluent or carrier and a tumor necrosis factor inhibiting amount of a compound selected from the group consisting of compounds of the formula (I) as defined hereinabove.

A preferred method of inhibiting production of TNF in a mammal in need thereof comprises administering to said mammal an effective amount of a compound selected from the group consisting of compounds of the formula (I) wherein A, Y, B and Z are as defined hereinabove for formula (I); R^1 is methyl or difluoromethyl; and R^2 is $(C_3\text{-}C_7)$cycloalkyl, $(C_6\text{-}C_9)$polycycloalkyl, phenylalkyl, phenoxyalkyl or indanyl,

where the alkyl portion of said alkyl, cycloalkyl, polycycloalkyl, phenylalkyl, phenoxyalkyl and indanyl may optionally be substituted with one or more fluorine atoms, -OH or $(C_1\text{-}C_4)$alkoxy,

and the aryl portion of said phenylalkyl, phenoxyalkyl and indanyl may optionally be substituted with $(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy or halogen.

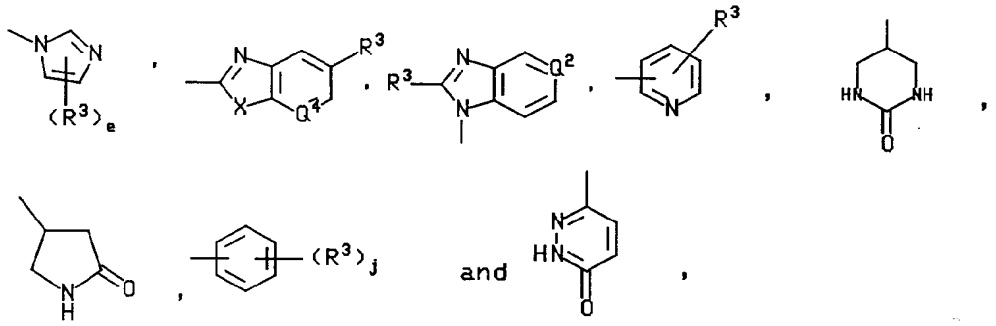
A more preferred method of inhibiting production of TNF in a mammal in need thereof comprises administering to said mammal an effective amount of a compound selected from the group consisting of compounds of the formula (I) wherein Z is as defined hereinabove for formula (I); A and B are independently selected from the group consisting of a covalent bond, $(C_1\text{-}C_5)$alkylene, $(C_2\text{-}C_5)$alkenyl and phenylene; Y is a covalent bond or O; R^1 is methyl or difluoromethyl; and R^2 is $(C_3\text{-}C_7)$cycloalkyl, $(C_6\text{-}C_9)$polycycloalkyl, phenylalkyl, phenoxyalkyl or indanyl,

where the alkyl portion of said alkyl, cycloalkyl, polycycloalkyl, phenylalkyl, phenoxyalkyl and indanyl may optionally

be substituted with one or more fluorine atoms, -OH or (C_1-C_4)alkoxy,

and the aryl portion of said phenylalkyl, phenoxyalkyl and indanyl may optionally be substituted with (C_1-C_4)alkyl, (C_1-C_4)alkoxy or halogen.

An even more preferred method of inhibiting production of TNF in a mammal in need thereof comprises administering to said mammal an effective amount of a compound selected from the group consisting of compounds of the formula (I) wherein A is covalent bond, methylene or cis-ethenyl; B is a covalent bond or phenylene; Z is selected from the group consisting of

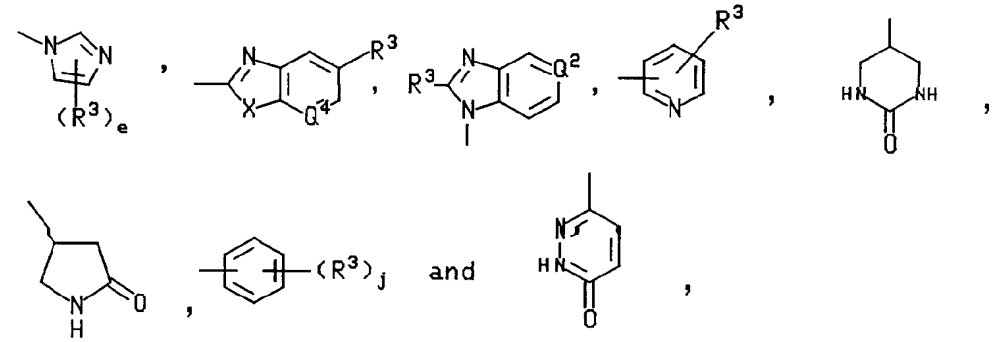


wherein R^3, X and e are as defined hereinabove for formula (I); j is 1 or 2; Q^4 is CH or N and Q^2 is CH or N; Y is a covalent bond or O; R^1 is methyl or difluoromethyl; and R^2 is (C_3-C_7)cycloalkyl, (C_6-C_9)polycycloalkyl, phenylalkyl, phenoxyalkyl or indanyl,

where the alkyl portion of said alkyl, cycloalkyl, polycycloalkyl, phenylalkyl, phenoxyalkyl and indanyl may optionally be substituted with one or more fluorine atoms, -OH or (C_1-C_4)alkoxy,

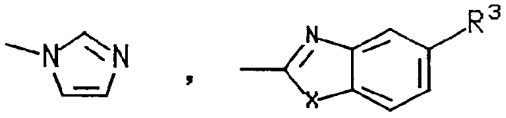
and the aryl portion of said phenylalkyl, phenoxyalkyl and indanyl may optionally be substituted with (C_1-C_4)alkyl, (C_1-C_4)alkoxy or halogen.

A most preferred method of inhibiting production of TNF in a mammal in need thereof comprises administering to said mammal an effective amount of a compound selected from the group consisting of compounds of the formula (I) wherein A is covalent bond, methylene or cis-ethenyl; B is a covalent bond or phenylene; Z is selected from the group consisting of

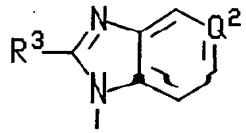


wherein X is as defined hereinabove for formula (I); j is 1 or 2; Q^4 is CH or N; Q^2 is CH or N; R^3 is (C_1-C_4)alkyl, CO_2H, $CONH_2$, nitro, $NHSO_2Me$, CF_3 or hydrogen; and e is 1; Y is a covalent bond or O; R^1 is methyl; and R^2 is cyclopentyl, norbornyl, indanyl, 1-phenylbut-3-yl, 1-phenoxyeth-2-yl, 1-phenylhex-5-yl or 1-phenylpent-4-yl.

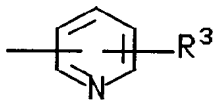
A further most preferred method of inhibiting production of TNF in a mammal in need thereof comprises administering to said mammal an effective amount of a compound selected from the group consisting of compounds of the formula (I) wherein Z is selected from the group consisting of



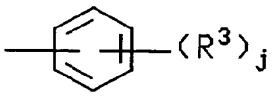
wherein R^3 is H, CO_2H or $CONH_2$ and X is as defined hereinabove for formula (I),



wherein R^3 is $(C_1\text{-}C_6)$alkyl and Q^2 is CH or N,



wherein R^3 is H, CO_2H or $CONH_2$, and

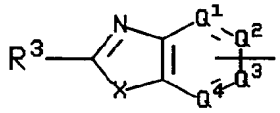


wherein R^3 is $(C_1\text{-}C_6)$alkyl, H, CO_2H, $CONH_2$ CF_3, NO_2 or $NHSO_2Me$ and j is 1 or 2; A is a covalent bond, methylene or cis-ethenyl; B is a covalent bond or phenylene; Y is a covalent bond or O; R^1 is methyl; and R^2 is cyclopentyl, norbornyl, indanyl, 1-phenylbut-3-yl, 1-phenoxyeth-2-yl, 1-phenylhex-5-yl or 1-phenyl-pent-4-yl.

As used throughout this specification and the appendant claims, the terms "alkyl" and "alkoxy" include both straight chain and branched groups; the term "halogen" includes fluoro, chloro and bromo; and the symbol "Ph" in the term "NCH_2Ph" means phenyl.

Those members of the substituent Z which are bicyclic are attached to the remainder of the compound of formula (I) through the ring of the Z substituent in which the bond is drawn.

As will be readily apparent to one skilled in the art, when Z is

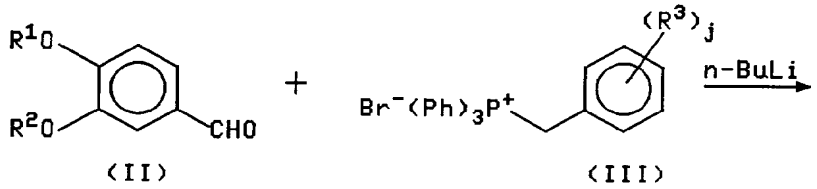


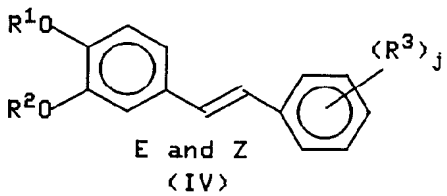
and one or more of Q^1, Q^2 Q^3 and Q^4 is N, Z cannot be bonded through one of its ring nitrogen atoms to the rest of the molecule.

Detailed Description of the Invention

The compounds utilized in the methods of the present invention having the formula (I) which comprise the racemic-diastereomeric mixtures and optical isomers of said compounds and the pharmaceutically acceptable salts thereof, are readily and generally prepared by the following reaction processes.

(a) In one process certain compounds of the formula (IV) can be prepared by the Wittig synthesis, according to the following reaction scheme:

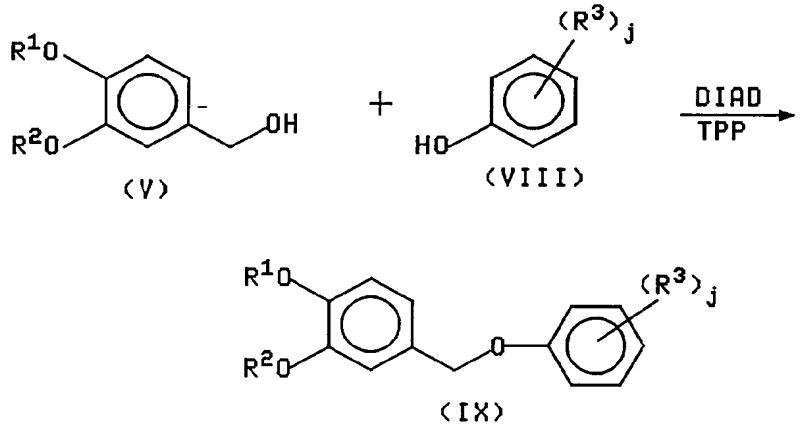




wherein R^1, R^2, R^3 and j are as defined above for formula (I).

In a typical procedure, approximately one equivalent of the phenylphosphonium bromide (III), dissolved or suspended in dry THF, is treated with about 1.1 equivalents of 2.5M n-BuLi in hexane. This mixture is allowed to stir at about -78°C for about one hour. Then approximately one equivalent of the aldehyde (II), dissolved in anhydrous THF, is added to the formed yilide solution at about -78°C. After about one hour of stirring at about -78°C, the reaction mixture is allowed to warm to room temperature over about 18 hours. The reaction is worked-up by pouring it into water and extracting twice with a solvent such as ethyl acetate. The ethyl acetate is evaporated and the crude product is chromatographed on silica gel using 15% ether/hexanes as the eluant to yield the desired compound (IV). Both the cis and trans isomers of (IV) are isolated.

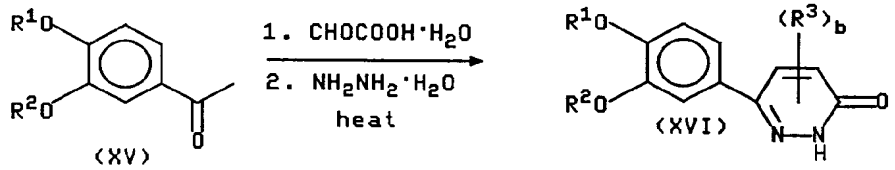
(b) In a further process, certain compounds of general formula (IX) can be prepared by a Mitsunobu type reaction, according to the following general reaction scheme:



wherein R^1, R^2, R^3 and j are as defined above for formula (I).

In a typical procedure, about 1 to 5 equivalents, typically 1.2 equivalents, of diisopropylazodicarboxylate (DIAD) or diethylazodicarboxylate (DEAD) is added to a mixture of about one equivalent of the alcohol (V), about one equivalent of the phenol (VIII) and about 1.1 equivalents of triphenylphosphine (TPP). All of the reactants are dissolved in a dry solvent, such as tetrahydrofuran. The reaction is stirred at room temperature for about 6 to hours, typically 18 hours. The solvent is evaporated and the crude oil is purified by column chromatography on silica gel to yield the compound of formula (IX).

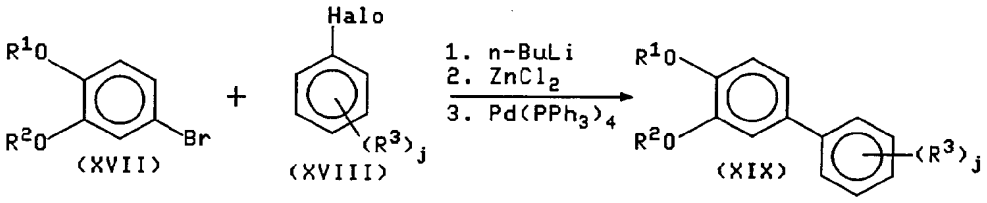
(c) Certain compounds of the formula (XVI) may be synthesized according to the scheme shown below:



wherein R^1, R^2, R^3 and b are as defined above for formula (I).

In a typical procedure, a ketone of the formula (XV) is heated with glyoxylic acid monohydrate at about 100°C to 150°C, preferably about 120°C. The reaction is cooled to about 60°C and about 2 ml of H_2O is added. About 20 to 30 drops of concentrated NH_4OH and about 1 equivalent of hydrazine monohydrate are added. The mixture is then heated at reflux for about 2 hours. It is cooled to room temperature and about 5 ml of water is added. The mixture is stirred for about 50 to 72 hours, preferably for about 60 hours. The suspension is filtered and purified by column chromatography on silica gel followed by crystallization.

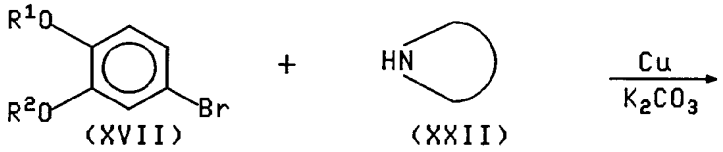
(d) Certain compounds of formula (XIX) are prepared by palladium cross coupling according to the following scheme:wherein R^1, R^2, R^3 and j are as defined

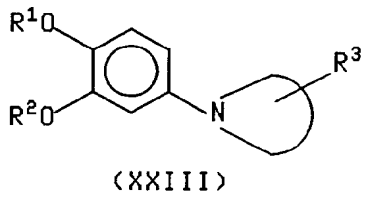


above for formula (I).

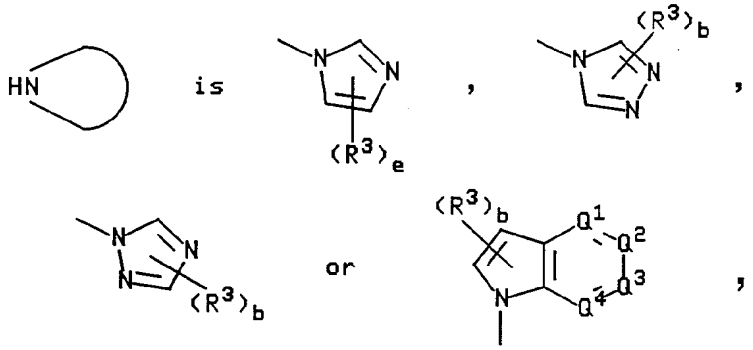
A typical procedure is carried out by taking a solution of about one equivalent of the appropriate bromo compound (XVII), dissolved in dry THF, and cooling it to about -78°C. About 1.1 equivalents of a 2.5M solution of n-BuU is added to the bromo compound and stirred for about 40 minutes at about -78°C. About 1.2 equivalents of a 1.0M solution of $ZnCl_2$ in ether is added and the reaction mixture allowed to warm to room temperature over about 35 minutes. A catalytic amount, about 0.05 equivalents, of tetrakis(triphenylphosphine)palladium(0) and the required halo compound (XVIII), wherein "Halo" is I, Br or Cl but preferably I or Br, are added to the reaction mixture and allowed to stir for about 12 hours. The reaction is concentrated and chromatographed on silica gel to yield the desired compound of formula (XIX).

(e) Certain compounds of formula (I) may also be synthesized by reaction of bromo compounds (XVII) with amino compounds (XXII), according to the general reaction scheme:





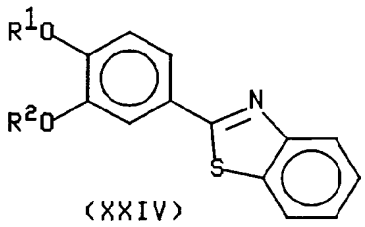
wherein R^1 and R^2 are as defined above for formula (I) and



wherein Q^1, Q^2, Q^3, Q^4, R^3, b and e are as defined above for formula (I).

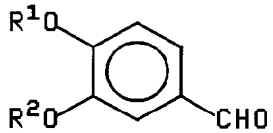
In a typical procedure, a mixture of about one equivalent of all of the reagents shown in the above scheme are heated to about 110-150°C for about 24 hours. The mixture is cooled to room temperature and worked-up according to standard methods well known to those skilled in the art. Chromatography on silica gel yields the desired compound of general formula (XXIII).

(f) The following procedure is employed to synthesize compounds of the formula



(XXIV)

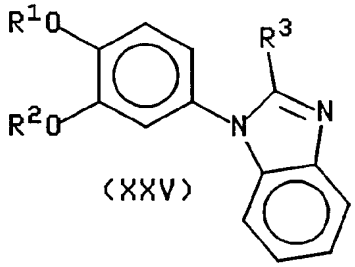
wherein R^1 and R^2 are as defined above for formula (I).
About one equivalent of an aldehyde of the formula



(II)

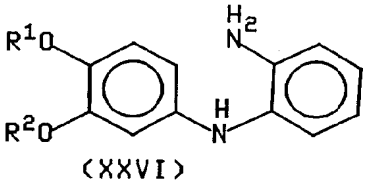
is mixed with about one equivalent of an optionally substituted 2-mercaptoaniline and heated on a steam bath for about 15 minutes. The reaction mixture is cooled and dissolved in a methanol solution of 10% $FeCl_3$ and stirred overnight. The reaction is diluted with H_2O and extracted with chloroform. The chloroform is evaporated and the residue is chromatographed to yield the desired benzothiazole derivatives of formula (XXIV).

(g) The following procedure is used to synthesize compounds of the formula



(XXV)

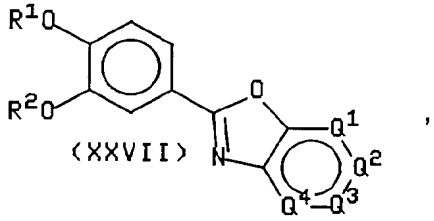
wherein R^1, R^2 and R^3 are as defined above for formula (I).
About one equivalent of a compound of the formula



(XXVI)

is mixed with ethyl formate and approximately 25 ml of formic acid and heated at about 100°C for about 18 hours. The solvent is evaporated and the residue chromatographed on silica gel to yield the desired benzimidazole derivatives of formula (XXV).

(h) Compounds having the general formula



(XXVII)

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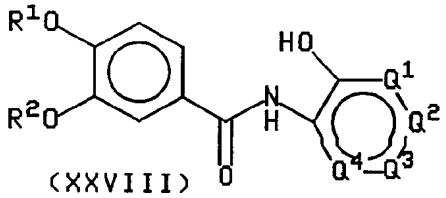
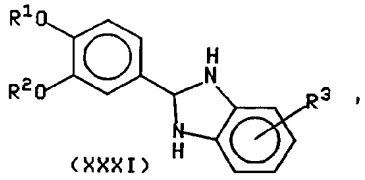
wherein R^1, R^2, Q^1, Q^2, Q^3 and Q^4 are as defined above for formula (I), are synthesized by the following general method. A compound of the general formula



(XXVIII)

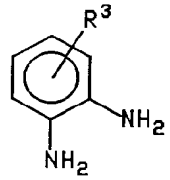
is mixed with $POCl_3$ and heated at reflux for about 24 hours. Excess $POCl_3$ is evaporated and the crude product is purified by chromatography on silica gel to yield the desired oxazolo derivatives of formula (XXVII).

(i) Compounds having the general formula



(XXXI)

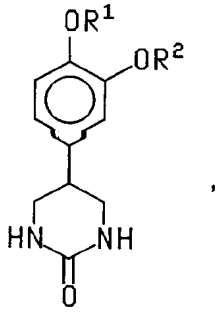
wherein R^1, R^2 and R^3 are as defined above for formula (I), are synthesized by the following general method. A compound of the general formula (II) is mixed with an appropriate compound of the general formula



(XXXII)

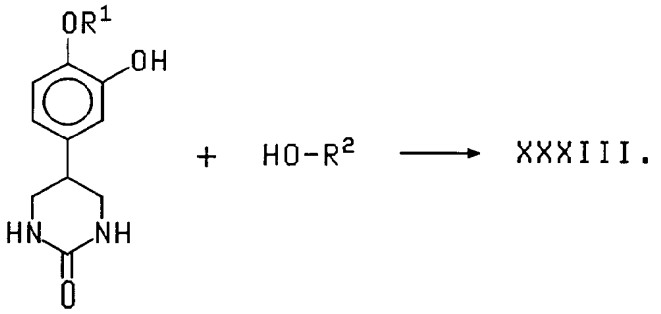
and the mixture heated to about 120°C for about 1 to 6 hours. The resulting residue is chromatographed on silica gel to yield the desired derivative of formula (XXXI).

(j) Compounds having the general formula



(XXXIII)

wherein R^1 and R^2 are as defined above for formula (I), are synthesized by one of the two general methods described below. The first general method is a Mitsinobu type reaction illustrated by the general scheme



(XXXIV)

The reaction is carried out analogously to the description provided in general method (e) above.

The second general method is carried out according to the following general scheme:

$$XXXIV + Halo\text{-}R^2 \rightarrow XXXIII,$$

wherein "Halo" is Cl, Br or I.

A compound of general formula (XXXIV) is dissolved in anhydrous DMSO. To this mixture approximately 2.5 equivalents of anhydrous K_2CO_3 and the appropriate halide (Halo-R^2) are added. The reaction mixture is heated to about 80°C for about 2-5 hours. After conventional work-up of the reaction mixture, the desired product is isolated by chromatography on silica gel.

As ascertained by one skilled in the art enabled by this disclosure, pharmaceutically-acceptable acid addition salts of certain compounds utilized in the present invention can be prepared which include, but are not limited to, those formed with HCl, HBr, HNO_3, H_2SO_4, H_3PO_4, CH_3SO_3H, p-$CH_3C_6H_4SO_3H$, CH_3CO_2H, gluconic acid, tartaric acid, maleic acid and succinic acid.

The ability of the compounds or the pharmaceutically acceptable salts thereof to inhibit TNF and, consequently, demonstrate their effectiveness for treating inflammatory conditions and diseases is shown by the following in vitro assay.

Lipopolysaccharide (LPS)-induced TNF Release From Human Monocytes Human Peripheral Blood Monocytes:

Venous blood from healthy volunteers is collected in 25 mM EDTA. Monocytes are separated by ficoll-hypaque and washed three times in complete HBSS (Hanks Balanced Salt Solution, available from GIBCO, Grand Island, NY). Cells are resuspended in a final concentration of 1.3×10^6 cells per mL in pre-warmed RPMI (available from GIBCO, Grand Island, NY) (containing 5% fetal calf serum, 2 mM glutamine, 100 units/ml penicillin/streptomycin antibiotic and 0.25 g/ml nystatin (all available from GIBCO, Grand Island, NY)). Monocytes (1 mL/well) are allowed to adhere to a 24- well Primaria Plate (coated tissue culture plates, available from VWR Scientific, South Plainfield, NJ) for 2 hours (37°C, 5% CO_2), after which time non-adherent cells are removed by gentle washing with RPMI.

Incubation:

Compounds are dissolved in DMSO. Each compound is tested at 4 concentrations. Fresh media (HBSS) (1.0 mL) and compound (10 µL) or DMSO control is added to each well. After 1 hour at 37°C, LPS (10 ng/mL final concentration) is added to appropriate wells. Plates are incubated overnight at 37°C. At the end of the incubation period, 250 µL of each culture supernatant is removed and duplicate 10 µL samples are tested at a 1:20 dilution for TNF activity by ELISA (available from Quantikine, R&D Operations, Minneapolis, MN) according to the manufacturer's instructions.

TNF is determined by interpolating the average absorbance onto a standard curve. Percent inhibition is determined by the following equation: (-[pg/mL TNF experimental/pg/mL TNF DMSO control]-1) x 100. IC_{50} is determined by linear regression of drug concentration plotted against inhibition and interpolation of the x value at y=50 using Biostat Linear Regression Program (available from Digital, Inc., Boston, MA).

For administration to humans to inhibit TNF in the treatment or alleviation of inflammatory conditions or disease, including but not limited to rheumatoid arthritis, osteoarthritis, asthma, bronchitis, chronic obstructive airways disease, psoriasis, allergic rhinitis, dermatitis and inflammatory bowel disease, sepsis, septic shock, tuberculosis, graft versus host disease and cachexia associated with AIDS or cancer, oral dosages of the compounds are generally in the range of from 0.1-500 mg daily for an average adult patient (70 kg). Thus for a typical adult patient, individual tablets or capsules contain from 0.1 to 50 mg of active compound, in a suitable pharmaceutically acceptable vehicle or carrier. Tablets or capsules can be given in multiple dosages to meet the dosage requirement. Dosages for intravenous administration are

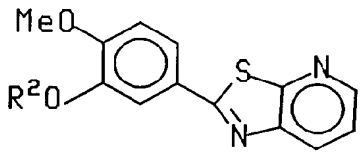
typically within the range of 0.1 to 10 mg per single dose as required. For intranasal or inhaler administration, the dosage is generally formulated as a 0.1 to 1% (w/v) solution. In practice the physician will determine the actual dosage which will be most suitable for an individual patient and it will vary with the age, weight and response of the particular patient. The above dosages are exemplary of the average case but there can, of course, be individual instances where higher or lower dosage ranges are merited, and all such dosages are within the scope of this invention.

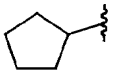
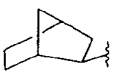
For human use, the compounds of the formula (I) can be administered alone, but will generally be administered in an admixture with a pharmaceutical diluent or carrier selected with regard to the intended route of administration and standard pharmaceutical practice. For example, they may be administered orally in the form of tablets containing such excipients as starch or lactose, or in capsules or ovales either alone or in admixture with excipients, or in the form of elixirs or suspensions containing flavoring or coloring agents. They may be injected parenterally; for example, intravenously, intramuscularly or subcutaneously. For parenteral administration, they are best used in the form of a sterile aqueous solution which may contain other substances; for example, enough salts or glucose to make the solution isotonic. For topical administration, they are best used in the form of solutions, lotions, ointments, salves and the like.

The following examples illustrate the synthesis of certain compounds used in the present invention. The following examples combined with the synthetic methodologies described immediately above enable those skilled in the art to make the compounds used in the present invention.

EXAMPLES 1 and 2

Reaction of the appropriate aldehyde with 2-mercapto-3-aminopyridine, analogous to the following procedure yielded the following compounds. A mixture of (2 mmoles) of an appropriate aldehyde and (2.1 mmoles) 2-mercapto-3-aminopyridine hydrochloride was heated on a steam bath for about 15 minutes. The resulting thick orange oil was cooled and dissolved in 5 ml of 10% $FeCl_3$ in methanol and allowed to stir overnight. The reaction was diluted with water and extracted with CH_2Cl_2. The CH_2Cl_2 layer was dried and evaporated to give a crude product which was purified on silica gel with CH_2Cl_2 to give the desired product. Recrystallization was performed to further purify the desired product.



Ex.#	R^2	M.P. °C	Analysis					
			Calculated %			Found %		
			C	H	N	C	H	N
1		118-120°	66.23	5.56	8.58	66.41	5.71	8.42
2		110-111°	--	--	--	--	--	--

EXAMPLE 3

6-[3-(Bicyclo[2.2.1]hept-2-yloxy)-4-methoxyphenyl]-3(2H)-pyridazinone

A mixture of 3-Exo-(±)-norbornyloxy-4-methoxyacetophenone (0.88 g, 3.38 mmol, 1.0 eq) and (0.30 g, 3.29 mmol, 0.95 eq) glyoxylic acid monohydrate was heated to about 120°C for about 2.2 hours. The light yellow melt was cooled to about 60°C and 2.0 ml of H_2O was added. Dissolution was brought on by addition of 25 drops of concentrated NH_4OH.

Hydrazine monohydrate (0.163 g, 3.29 mmol, 0.95 eq) was added and the reaction mixture heated to reflux for about 2 hours. The reaction mixture was cooled to room temperature, 5 ml of H_2O was added to it, and the mixture stirred for about 60 hours at room temperature. The resulting suspension was filtered, washed with H_2O and air dried to yield 0.87 g of a creamy yellow solid. Silica gel chromatography eluting with 5% CH_3OH-CH_2Cl_2, followed by recrystallization from isopropanol-hexane gave 0.50 g, 49%, of off-white crystals. M.P.: 188-189°C. Elemental Analysis Calc'd for $C_{18}H_{20}N_2O_3$: Calc'd: C, 69.21; H, 6.45; N, 8.95. Found: C, 68.92; H, 6.42; N, 8.88.

EXAMPLE 4

1-[3-(Cyclopentyloxy)4-methoxy-phenyl]-1H-imidazo[4,5-c]pyridine

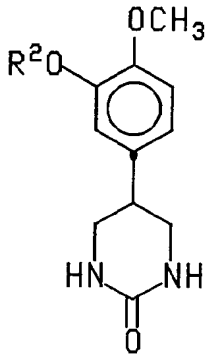
A solution of 2.05g of 1-(3-hydroxy-4-methoxyphenyl)-1H-imidazo[4,5-c]pyridine, 2.5 g of cyclopentylbromide and 665 mg of NaH in 20 ml of DMF was stirred at room temperature overnight. The reaction was poured into water and extracted with ethyl acetate, dried to give 1.4 g of crude product. Recrystallization from CH_2Cl_2 gave 574 mg product. M.P.: 66-68°C.

EXAMPLE 5

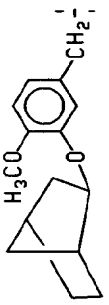
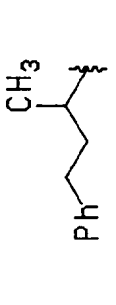
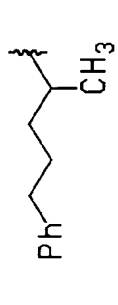
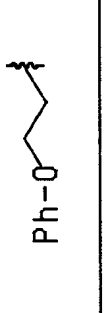
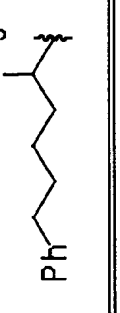
Tetrahydro-5-[3-(4-phenylbutoxy)4-methoxyphenyl]-2(1H)-pyrimidinone

Diisopropylazodicarboxylate (1.1 ml, 5.70 mmol,1.2 eq) was added to a mixture of (1.06 g, 4.75 mmol, 1.0 eq) tetrahydro-5-(3-hydroxy-4-methoxyphenyl)-2(1H)-pyrimidinone, (1.37 g, 5.23 mmol,1.1 eq)triphenylphosphine, and (714 mg, 4.75 mmol, 1.0 eq) 4-phenyl-1-butanol in 20 ml of anhydrous tetrahydrofuran. After heating to reflux for about 18 hours, the reaction mixture was cooled to room temperature, diluted with 350 ml ethyl acetate washed twice with 1N NaOH, once with H_2O, once with brine, dried over Na_2SO_4, and concentrated to yield an orange solid. Silica gel chromatography eluting with 4% CH_3OH-CH_2Cl_2 yielded 527 mg of a white solid, which was recrystallized from ethyl acetate to afford 480 mg, 29%, of white needles. M.P.: 142-143°C. Elemental Analysis Calc'd for $C_{21}H_{26}N_2O_3$: Cald: C, 71.17; H, 7.40; N, 7.90. Found: C, 71.12; H, 7.32; N, 7.75.

EXAMPLES 6-10

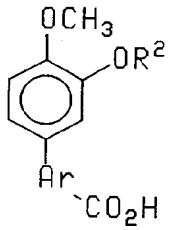


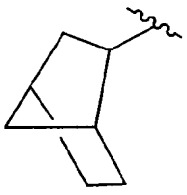
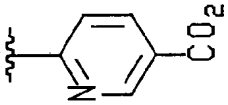
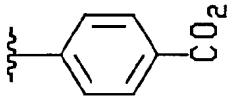
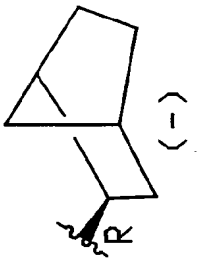
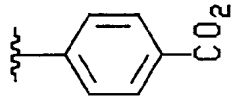
Reaction of 2 (1H)-pyrimidine, tetrahydro-5-(3-hydroxy-4-methoxyphenyl)-with the appropriate alcohol of the general formula R-OH, analogous to the procedure of Example 5, yielded the following compounds:

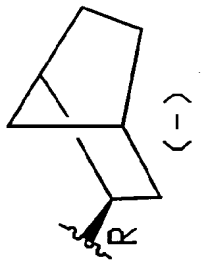
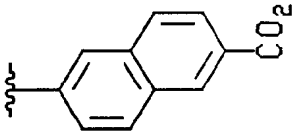
Ex.#	R^2	M.P. °C	Analysis					
			Calculated (%)			Found (%)		
			C	H	N	C	H	N
6		157-60°	69.01	7.13	6.19	67.58	6.76	6.33
7		152-4°	71.17	7.40	7.90	71.13	7.42	7.80
8		99-101°	--	--	--	--	--	--
9		147-9°	--	--	--	--	--	--
10		90-2°	72.22	7.91	7.32	72.20	7.79	7.27

EXAMPLES 11-14

Reaction of the appropriate bromocatechol with the proper halo aromatic ester of the formula X-Ar-CO-OR^4 followed by hydrolysis analogous to the following procedure yielded the desired products. To a solution of 1.0 eq an appropriate bromocatechol in 30 ml of dry THF at about -78°C was added 1.1 eq 2.5M n-BuLi. After stirring for about 15 minutes at about -78°C, 1.2 eq of 1.0M $ZnCl_2$ in ether was added and the mixture allowed to warm to room temperature over about 35 minutes. Tetrakis(triphenylphosphine)palladium(0) (0.05 eq) and 1.0 eq of a halo aromatic ester of the formula X-Ar-CO-OR^4 were added to the reaction and the mixture allowed to stir at room temperature for about 2.5 hours. The reaction mixture was concentrated in vacuo, costripped with $CHCl_3$, and chromatographed on a silica gel column eluting with ethyl acetate-hexane (0-10%). Hydrolysis of the ester was accomplished as follows. A mixture of 1.0 eq the ester in 8 ml methanol and 2.0 eq of 1N NaOH was heated to reflux for about 1.5 hours. The reaction mixture was cooled to room temperature, concentrated in vacuo, poured into 100 ml H_2O, basified to pH 12, and washed once with ethyl acetate. The aqueous layer was acidified to pH 4 and extracted three times with ethyl acetate. The ethyl acetate extracts were combined, washed once with H_2O, once with brine, dried over Na_2SO_4, and concentrated to yield the following compounds of the general formula:



Ex.#	R^2	$ArCO_2H$	M.P. °C	Analysis					
				Calculated %			Found %		
				C	H	N	C	H	N
11			221-3°	70.78	6.24	4.13	70.60	6.08	4.02
12			230-32°	73.05	6.47	--	73.16	6.51	--
13			234-6°	74.53	6.55	--	74.49	6.24	--

Ex.#	R^2	$ArCO_2H$	M.P. °C	Analysis					
				Calculated %			Found %		
				C	H	N	C	H	N
14			242-4°	77.30	6.23	--	77.28	6.25	--

EXAMPLE 15

2-[(4-Methoxy-4'-nitro[1,1'-biphenyl]-3-yl)oxy]bicyclo[2.2.1]heptane

To a stirred solution of (2 g, 6.73 mmol, 1.0 eq) (±)-1-methoxy-2-exo-norbornyloxy-4-bromobenzene in 50 ml of dry THF at about -78°C was added 2.96 ml (7.40 mmol, 1.1 eq) 2.5M n-BuLi. After about 45 minutes at about -78°C, (8.07 ml, 8.07 mmol, 1.2 eq) 1.0M $ZnCl_2$ in ether was added and the reaction mixture allowed to warm to room temperature over about 30 minutes. $Pd(PPh_3)_4$ (389 mg, 0.34 mmol, 0.05 eq) and then (1.67 g, 6.73 mmol, 1.0 eq) 1-nitro-4-iodobenzene were added and the reaction mixture stirred for about 30 minutes at room temperature. The mixture was concentrated in vacuo and chromatographed on silica gel, eluting with ethyl acetate/hexane (0-8%) to afford 1.32 g, 58%, of a yellow solid. M.P.: 134-135°C.

EXAMPLE 16

N-(3'-Bicyclo[2.2.1]hept-2-yloxy)-4'-methoxy-[1,1'-biphenyl]-4-ylmethanesulfonamide

To a stirred solution of (525 mg, 1.70 mmol, 1.0 eq) 3'-(bicyclo[2.2.1]hept-2-yloxy)-4'-methoxy[1,1'-biphenyl]-4-amino in 10 ml dry CH_2Cl_2 at about 0°C was added 0.28 ml of triethylamine (2.03 mmol, 1.2 eq), followed by 355 mg (2.03 mmol, 1.2 eq) methanesulfonic anhydride. The mixture was stirred at about 0°C for about 10 minutes, then at room temperature for about 1 hour, at which point an additional 200 mg (1.1 mmol, 0.7 eq) of methane sulfonic anhydride was added. After stirring an additional 30 minutes at room temperature, the reaction mixture was concentrated in vacuo, costripped twice with $CHCl_3$, and chromatographed on silica gel eluting with ethyl acetate-hexane (10-35%) to yield 700 mg of compound. Recrystallization from ethyl acetate/hexane afforded 650 mg, 98%, of crystals. M.P.: 151-153°C. Elemental Analysis Calc'd for $C_{21}H_{25}NO_4S$: Calc'd: C, 65.08; H, 6.51; N, 3.61. Found: C, 64.92; H, 6.21; N, 3.53.

EXAMPLE 17

2-[3-[2-indoxy]-4-methoxyphenyl]-1H-imidazo[4,5-b]pyridine

To a magnetically stirred solution of 3-(2-indoxy)-4-methoxybenzaldehyde (3.0 g, 11.2 mmoles) in acetone (50 ml) was added 7 ml of 2.67 M solution of Cr_2O_3 in 50% aqueous H_2SO_4. This was exothermic enough to effect a mild reflux of acetone, and no external cooling was necessary. After stirring overnight at ambient temperature, 50 ml of H_2O was added, and the acetone was allowed to evaporate over a steam bath. The crude product was filtered and washed with 1 N HCl followed by water. Recrystallization from isopropyl ether gave 1.9 g of 3-(2-indoxy)-4-methoxybenzoic acid as off-white crystals. M.P.: 189-191°C.

A solution of 0.50 g of 3-(2-indoxy)-4-methoxybenzoic acid in 10 ml of thionyl chloride was heated at reflux for about 1 hour. Removal of the volatiles under reduced pressure gave 3-(2-indoxy)-4-methoxybenzoyl chloride as a dull pink solid which was immediately used in the next step without purification.

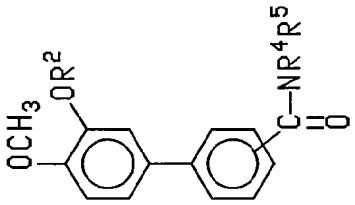
To a magnetically stirred solution of 2,3-diaminopyridine (1.8 mmole) in dry pyridine (15 ml) at about 0°C was added dropwise a solution of 3-(2-indoxy)-4-methoxybenzoyl chloride in dry THF (10 ml). After about 1 hour the mixture was warmed to ambient temperature and after about 16 hours the volatiles were removed under reduced pressure. The residue was suspended in 25 ml of water, filtered, and washed with water to give 0.59 g of a white solid. M.P.: 226-228°C (dec).

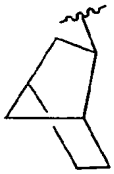
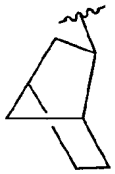
The above amide was suspended in 10 ml of phosphorous oxychloride and heated at reflux for about 1.5 hours, at which time the reaction mixture was homogeneous. The volatiles were removed under reduced pressure, and the residue was suspended in 25 ml of saturated sodium bicarbonate, filtered, and air-dried. Column chromatography followed by recrystallization from ethanol gave 180 mg of off- white crystals. M.P.: 206-208°C. Elemental analysis calculated for $C_{22}H_{19}O_2N_3$: C, 73.93; H, 5.36; N, 11.76. Found: C, 73.01; H, 5.06; N, 11.76.

EXAMPLES 18-19

Reaction of the appropriate carboxylic acid with the proper amine of the general formula NR_1R_2, analogous to the following procedure yielded the desired compounds. A suspension of an appropriate carboxylic acid (1.38 mmoles) in dry methylene chloride was treated with excess thionyl chloride (6.93 mmoles) and a catalytic amount of anhydrous DMF (3-5 drops). The resulting clear solution was heated to reflux under nitrogen atmosphere for about 1 hour. The methylene chloride was removed in vacuo and the resulting solid residue azeotroped with an additional 15 ml of dry methylene chloride. The residue was dissolved in 15 ml of dry CH_2Cl_2, cooled to about 0°C (ice bath) and dry anhydrous ammonia gas bubbled directly into the reaction mixture for approximately 5 minutes. This was followed by allowing the

reaction to stir at about 0°C for an additional hour, after which time the reaction mixture was diluted with 500 ml of ethyl acetate and 300 ml of H_2O. The organic layer was separated and washed with 1N HCl (2 x 350 ml), 2N NaOH (2 x 350 ml), water (1 x 300 ml), brine, dried over $MgSO_4$ and evaporated under reduced pressure which yielded the following compounds:



Ex.#	R^2	R^1	R^5	Position of Amide	M.P. °C	Analysis					
						Calculated %			Found %		
						C	H	N	C	H	N
18		H	H	Meta	151-153°	74.75	6.87	4.15	74.47	6.97	4.00
19		H	H	Para	245-247°	--	--	--	--	--	--

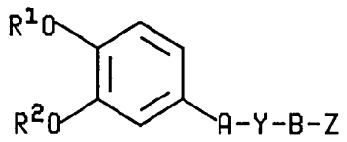
EXAMPLE 20

cis-1-[4-[2-[3-(Cyclopentyloxy)-4-methoxyphenyl]-ethenylphenyl]-2-methyl-1H-imidazo[4,5-c]pyridine

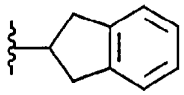
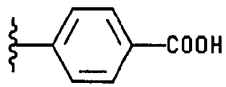
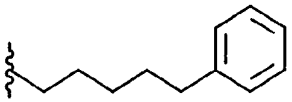
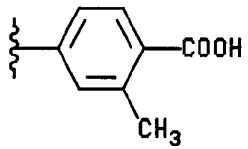
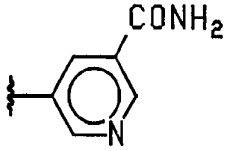
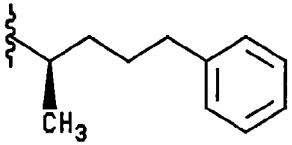
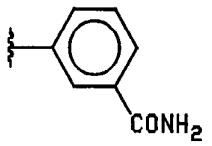
To a stirred suspension of (1.74 g, 3.13 mmol, 1.2 eq) [[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]triphenylphosphonium bromide in 20 ml dry tetrahydrofuran at about -50°C was added (1.1 ml, 2.78 mmol, 1.1 eq) of 2.5M n-BuLi. The mixture was warmed to about 0°C over about 1 hour, cooled to about -78°C, and a solution of (600 mg, 2.53 mmol, 1.0 eq) 4-(2-methyl-1H-imidazo[4,5-c]pyridin-1-yl)benzaldehyde in 20 ml dry tetrahydrofuran was added dropwise over about 10 minutes. The reaction mixture was allowed to warm to room temperature over about 18 hours then was quenched with 10 ml saturated NH_4Cl solution. The mixture was poured into 200 ml of H_2O and extracted twice with ethyl acetate. The ethyl acetate extracts were combined, washed once with H_2O, once with brine, dried over $MgSO_4$, and concentrated to give 2 g of an oil. Flash chromatography eluting with 65% acetone-hexane gave 403 mg of crude product, which was recrystallized from ether-hexane to yield 305 mg, 36%, of the cis product. The cis-product M.P.: 123-125°C. Elemental Analysis of the cis-product: Calc'd for $C_{27}H_{27}N_3O_2$: Calc'd: C, 76.21; H, 6.40; N, 9.87. Found: C, 76.14; H, 6.34; N, 9.71.

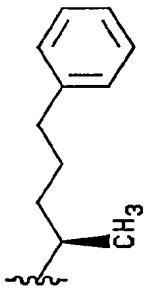
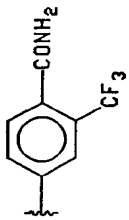
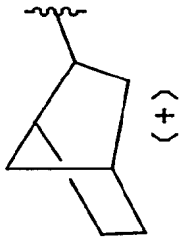
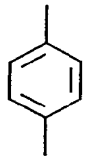
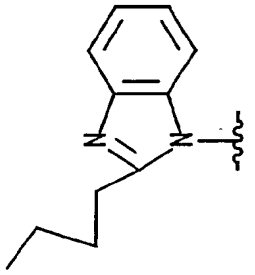
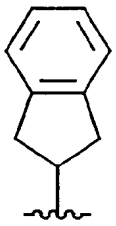
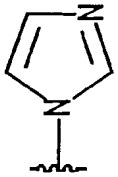
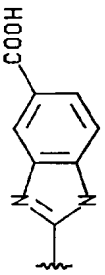
EXAMPLES 21-31

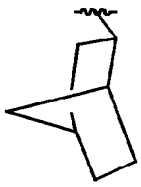
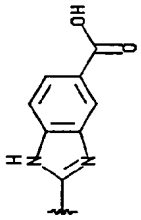
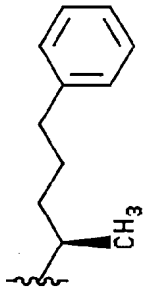
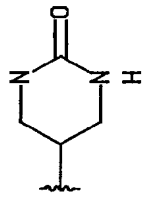
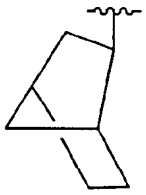
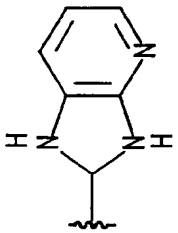
Additional examples, which were prepared according to the methods described and readily apparent to those skilled in the art, are shown in the following table.



*C.B.= Covalent Bond

Ex. #	R^1	R^2	A	Y	B	Z-R^3	M.P.(°C)
21	CH_3		C.B.	C.B.	C.B.		244-247
22	CH_3		C.B.	C.B.	C.B.		127-128
23	CH_3		C.B.	C.B.	C.B.		169-171
24	CH_3	 (+)	C.B.	C.B.	C.B.		88-90

Ex. #	R^1	R^2	A	Y	B	$Z\text{-}R^3$	M.P.(°C)
25	CH_3		C.B.	C.B.	C.B.		79-81
26	CH_3		$-CH_2-$	-O-			129-131
27	CH_3		C.B.	C.B.	C.B.		118-119
28	CH_3		C.B.	C.B.	C.B.		185-187

Ex. #	R^1	R^2	A	Y	B	$Z\text{-}R^3$	M.P.(°C)
29	CH_3		C.B.	C.B.	C.B.		221-223
30	CH_3		C.B.	C.B.	C.B.		131-133
31	CH_3		C.B.	C.B.	C.B.		153-154

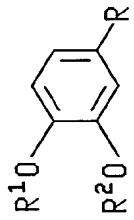
Preparation 1

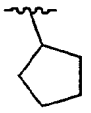
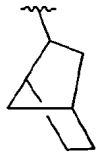
3-(Bicyclo[2.2.1]hept-2-yloxy)-4-methoxybenzaldehyde

Diisopropylazodicarboxylate (7.8 ml, 39.5 mmol, 1.2 eq) was added neat to a 25° solution of (5.00 g, 32.9 mmol,1.0 eq) 3-hydroxy-4-methoxybenzaldehyde (9.48 g, 36.1 mmol, 1.1 eq) triphenylphosphine, and (3.69 g, 32.9 mmol, 1.0 eq) (±)-endo-norborneol in 100 ml of anhydrous tetrahydrofuran. After refluxing for 6 hours, the reaction mixture was poured into 1 liter of H_2O and extracted twice with ethyl acetate. The ethyl acetate layers were combined and washed twice with H_2O, once with 1N NaOH, once with H_2O and once with brine and then the solution was dried over anhydrous sodium sulfate. Filtration, concentration, and drying afforded 26.1 g of crude product, which was chromatographed on a silica gel column, eluting with 20% ethyl acetate-hexane to afford 5.68 g, 70% yield, of a yellow oil. IR(cm^{-1}): 1680,1580. NMR ($CDCl_3$): δ 9.82 (s, 1H), δ 4.27 (d, 1H). High resolution mass spectra (HRMS): 246.1300.

PREPARATIONS 2-8

Reaction of the appropriate vanillin with the requisite alcohol of the formula R^2-OH, analogous to the procedure of Preparation 1, afforded the following compounds:



Prep.#	R¹	R	R²	M.P. °C	M.W.	Mass Spec (M+)	Analysis			
							Calculated (%)		Found (%)	
							C	H	C	H
2	CH_3	-CHO		oil	220.3	220	--	--	--	--
3	CH_3			oil	260.3	260	73.82	7.74	73.19	8.03
			sm = endo prod = exo							

Preparation 4

Bis(2-methoxy-5-bromophenyl)carbonate

Dissolved (8.26 ml, 160 mmol, 2.2 eq) bromine in 10 ml of $CHCl_3$ and then added it dropwise over 10 minutes to (20.0 g, 72.9 mmol, 1.0 eq) of bis(2-methoxy-phenyl)carbonate in 60 ml of $CHCl_3$ at room temperature. Stirred for 60 minutes at room temperature, then filtered the reaction mixture, washing the precipitate three times with $CHCl_3$ and once with hexane. The precipitate was recrystallized from $CHCl_3$ to yield 20.7 g, 66% yield, of bis(2-methoxy-5-bromophenyl)carbonate as white prisms.

Preparation 5

5-Bromoguaiacol

A suspension of (20.7 g, 47.9 mmol, 1.0 eq) bis(2-methoxy-5-bromophenyl)-carbonate in 250 ml methanol and 60 ml (120 mmol, 2.5 eq) of 2N NaOH was refluxed for 2 hours. The reaction mixture was cooled to room temperature, concentrated to a volume of ca 100 ml, and poured into 1 L of H_2O. The pH was adjusted to 2 using 1 N HCl. The acidic mixture was transferred to a separatory funnel, and extracted three times with ether. The ether extracts were combined and washed once with H_2O, once with brine, and then dried over anhydrous sodium sulfate. Filtration, concentration and drying afforded 19.0 g of a white solid, which was recrystallized from petroleum ether to yield 17.63 g, 91% yield, of white prisms.

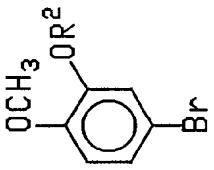
Preparation 6

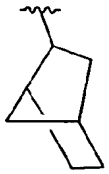
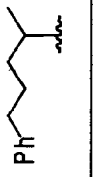
2-(5-Bromo-2-methoxyphenoxy)bicyclo[2.2.1]heptane

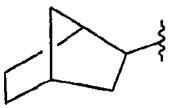
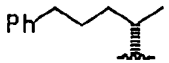
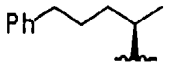
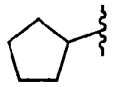
Neat diethylazodicarboxylate (1.4 ml, 8.87 mmol, 1.2 eq) was added to a 25°C solution of (1.50 g, 7.39 mmol, 1.0 eq) 5-bromoguaiacol, (2.13 g, 8.13 mmol, 1.1 eq) triphenylphosphine and (0.829 g, 7.39 mmol, 1.0 eq) of S(-)endo-norborneol in 25 ml of anhydrous tetrahydrofuran. After stirring 18 hours at room temperature under N_2, the reaction mixture was diluted with 350 ml of ether, washed twice with 1 N NaOH, once with H_2O, once with brine, and then dried over anhydrous Na_2SO_4. Filtration, concentration and drying afforded a yellow oil which was triturated with ca 250 ml of 1:1 ether-hexane to remove triphenylphosphine oxide. The filtrate was concentrated in vacuo, and chromatographed on a silica gel column, eluting with 10% ethyl acetate-hexane, to afford 1.75 g, 80% yield, of a clear, colorless oil. Elemental Analysis: Calc'd for $C_{14}H_{17}O_2Br$: Calc'd: C, 56.57; H, 5.77%. Found: C, 56.68; H, 5.73%.

Preparations 7-13

Reaction of 5-bromoguaiacol with the requisite alcohol of the formula R^2-OH, analogous to the procedure of Preparation 11, afforded the following compounds:



Prep.#	R^2	M.P. °C	M.W.	Mass Spec (M+)	Analysis			
					Calculated (%)		Found (%)	
					C	H	C	H
7	 endo = sm exo = prod	oil	297.3	298	--	--	--	--
8		oil	349.3	350	--	--	--	--

Prep.#	R^2	M.P. °C	M.W.	Mass Spec (M+)	Analysis			
					Calculated (%)		Found (%)	
					C	H	C	H
9	 R(+) = sm S(+) = prod	oil	297.2	298	56.57	5.77	56.74	5.72
10	 R(-) = sm S(+) = prod	oil	349.29	349.2	61.89	6.09	61.18	6.10
11	 S(+) = sm R(+) = prod	oil	349.29	349.2	61.89	6.09	59.77	5.66
12		oil	271.17	271.1	53.16	5.58	53.41	5.62

Prep.#	R^2	M.P. °C	M.W.	Mass Spec (M+)	Analysis			
					Calculated (%)		Found (%)	
					C	H	C	H
13		oil	335.26	--	--	--	--	--

*sm = starting material
prod = product

Preparation 14

3-Cyclopentyl-4-methoxybenzoic acid

To a stirred suspension of (5.0 g, 27 mmol, 1.0 eq) methyl vanillate, (2.5 ml, 27 mmol, 1.0 eq) cyclopentanol, and (7.4 g, 28 mmol, 1.05 eq) triphenylphosphine in 40 ml of anhydrous tetrahydrofuran was added (4.7 ml, 29.7 mmol, 1.1 eq) of diethylazodicarboxylate. The reaction mixture was stirred 18 hours at room temperature, concentrated in vacuo, and flash chromatographed on a silica gel column, eluting with 20% ethyl acetate/hexane, to yield 7.0 g, > 100%, of an oil, methyl-3-methoxy-4-cyclopentyl-oxybenzoate.

A mixture of (7.0 g, 27 mmol, 1.0 eq) methyl-3-methoxy-4-cyclopentyloxy benzoate, 8 ml (42 mmol, 1.5 eq) 5N NaOH and 40 ml MeOH was refluxed for 3 hours. The mixture was concentrated to ca 20 ml, poured into 400 ml H_2O (pH 10) and washed twice with ether. The aqueous layer was acidified to pH 1 and extracted twice with ether. The ether extracts were combined, washed once with H_2 O, once with brine, dried over $MgSO_4$ and then concentrated to yield 6 g of a white solid. Recrystallization from ether-hexane yielded 5.60 g, 88%, of white crystals. Elemental Analysis: Calcd. for $C_{13}H_{16}O_4$: Calc'd: C, 66.09; H, 6.83. Found: C, 66.20; H, 6.64.

Preparation 14

2-Butyl-3-(4-hydroxyphenyl)benzimidazole

A mixture of (8.0 g, 51 mmol, 1.0 eq) 1-chloro-2-nitrobenzene and (5.54 g, 51 mmol, 1.0 eq) 4-aminophenol in 40 ml of dry dimethylsulfoxide was heated to reflux for 18 hours. The reaction mixture was cooled, poured into 400 ml of 0.1N HCl and 400 ml ethyl acetate, stirred, and filtered through celite. The filtrate layers were separated, and the aqueous layer was extracted with ethyl acetate. The ethyl acetate extracts were combined, washed twice with H_2O, once with brine, dried over $MgSO_4$, and concentrated to give 8 g of a dark oil. Silica gel chromatography eluting with 20% ethyl acetate/hexane gave 1.63 g, 14%, of a red solid.

A mixture of (1.6 g, 6.89 mmol, 1.0 eq) 4-N-(2-nitrophenyl)amino phenol and 800 mg of 10% Pd/C in 100 ml ethyl acetate was placed on a Parr hydrogenation apparatus and shaken under 50 psi H_2 for 3 hours. The mixture was filtered through celite, concentrated in vacuo, and chromatographed on a silica gel column eluting with 50% ethyl acetate/hexane to give 1.3 g, 94%, of an orange-yellow solid.

A mixture of (600 mg, 3.00 mmol, 1.0 eq) 4-N-(2-aminophenyl)amino phenol and 10 ml valeric anhydride was heated to reflux for 18 hours. The mixture was taken up in 50 ml of methanol, basified with 2N NaOH to pH 10, and stirred 1 hour at room temperature. The reaction mixture was then neutralized and extracted twice with ethyl acetate. The ethyl acetate extracts were combined, washed twice with H_2O, once with brine, dried over $MgSO_4$ and concentrated to give 1 g of an oil. Silica gel chromatography eluting with 2½% CH_3OH-CH_2Cl_2 gave 124 mg, 16%, solid. M.P.: 192-194°C.

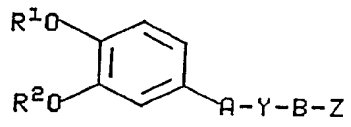
Preparation 15

4-[(5-Bromo-2-methoxy)phenoxy]butanoic acid ethyl ester

A mixture of 15.0 g (0.0740 mol) of 2-methoxy-4-bromophenol, 17.4 g (0.0890 mol) of ethyl 4-bromobutyrate, 20.5 g (0.148 mol) or K_2CO_3, and 200 ml of DMF was stirred at about 80°C was continued for about 16 h. The combined ether extracts were washed with brine (1 x 300 ml), dried ($MgSO_4$), and evaporated to give 26.0 g of an orange oil. Purification by flash chromatography using an ethyl acetate-hexane (1:4) eluant gave 19.7 g (84%) of the title compound as a clear oil (R_f 0.5 EtOAc-hexane, 3:7). ^{1}H-NMR ($CDCl_3$) δ 1.25 (3H, t, J=7), 2.09-2.18 (2H, m), 2.51 (2H, t, J=7), 3.82 (3H, s), 4.03 (2H, t, J=7), 4.13 (2H, q, J=7), 6.72 (1H, d, J=8), 6.97-7.08 (2H, m).

Claims

1. The use of a compound selected from the group consisting of compounds of the formula (I)



(I)

the racemic-diastereomeric mixtures and optical isomers of said compounds and the pharmaceutically acceptable salts thereof wherein

R^1 is selected from the group consisting of methyl, ethyl, difluoromethyl and trifluoromethyl;

R^2 is selected from the group consisting of $(C_1\text{-}C_6)$alkyl, alkoxyalkyl having 3 to 7 carbons in the alkoxy portion and 2 to 4 carbons in the alkyl portion, phenoxyalkyl having 2 to 6 carbons in the alkyl portion, $(C_3\text{-}C_7)$cycloalkyl, $(C_6\text{-}C_9)$ polycycloalkyl, phenylalkyl having 1 to 8 carbons in the alkyl portion, Phenylaminoalkyl having 2 to 6 carbons in the alkyl portion and the amino may be optionally substituted with $(C_1\text{-}C_4)$ alkyl and indanyl,

where the alkyl portion of said alkyl, phenoxyalkyl, cycloalkyl, polycycloalkyl, phenylalkyl and indanyl may optionally be substituted with one or more fluorine atoms, -OH or $(C_1\text{-}C_4)$alkoxy,

and the aryl portion of said phenylalkyl, phenoxyalkyl and indanyl may optionally be substituted with $(C_1\text{-}C_4)$ alkyl, $(C_1\text{-}C_4)$alkoxy or halogen;

A and B are independently selected from the group consisting of a covalent bond, optionally substituted $(C_1\text{-}C_5)$ alkylene, optionally substituted $(C_2\text{-}C_5)$alkenyl and optionally substituted phenylene,

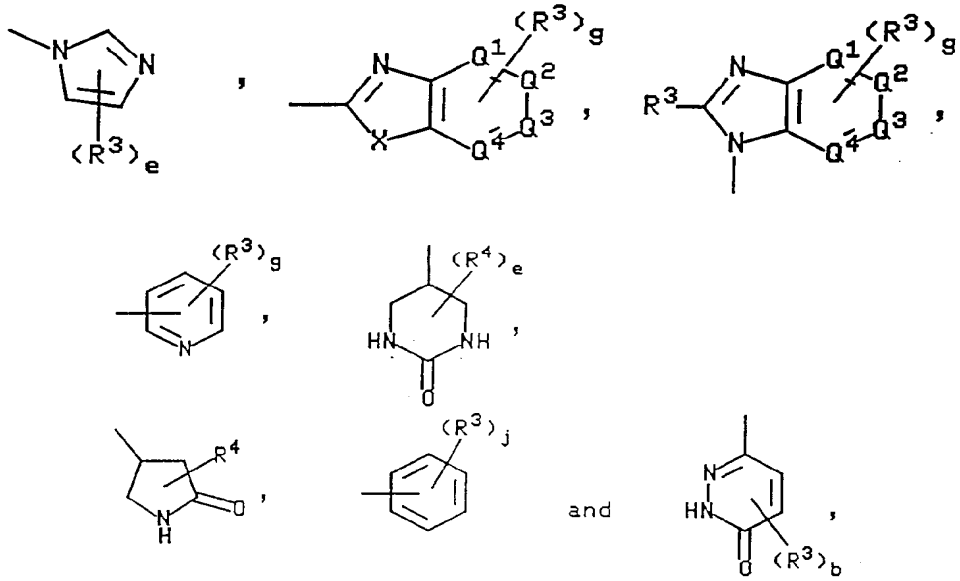
where said optionally substituted alkylene may be monosubstituted and each substituent is selected from the group consisting of oxo, $(C_1\text{-}C_4)$alkoxy, CO_2R^6 and hydroxy,

said optionally substituted alkenyl may be monosubstituted with $(C_1\text{-}C_4)$alkoxy or CO_2R^6, and

said optionally substituted phenylene may be monosubstituted with $(C_1\text{-}C_4)$alkoxy, CO_2R^6 or hydroxy, wherein R^6 is hydrogen or $(C_1\text{-}C_4)$alkyl;

Y is selected from the group consisting of a covalent bond, O, NR^6 and S wherein R^6 is as defined above;

Z is selected from the group consisting of



where Q^1, Q^2, Q^3, and Q^4 are independently N, CH or, when also bonded to B, C and provided that at least two of Q^1, Q^2, Q^3, and Q^4 are not N;

X is selected from the group consisting of NR^4 and S;

e is an integer from 1 to 3;

g is an integer from 1 to 4;

j is an integer from 1 to 5;

each R^3 is independently selected from the group consisting of hydrogen, halogen, CF_3, $(C_1\text{-}C_6)$alkyl, $CH(R^7)$ CO_2R^4, $(C_1\text{-}C_6)$alkoxy, CO_2R^4, $CONR^4R^5$, CONHOH, $CH_2NR^4R^5$, NR^4R^5, nitro, hydroxy, CN, SO_3H, phenylalkyl

having 1 to 4 carbons in the alkyl portion, $SO_2NR^4R^5$, $N(SO_2R^8)_2$ and $NHSO_2R^8$,

where R^4 for each occurrence is independently selected from the group consisting of hydrogen, $(C_1\text{-}C_6)$alkyl, phenyl optionally substituted with $(C_1\text{-}C_4)$alkyl or halogen, $CH(R^7)CO_2R^6$, $(C_3\text{-}C_7)$cycloalkyl, phenylalkyl having 1 to 4 carbons in the alkyl portion and dialkylaminoalkyl having a total of 5 carbons in the dialkylamino portion and having 2 to 5 carbons in the alkyl portion where R^6 is as defined above,

R^5 for each occurrence is independently selected from-the group consisting of hydrogen, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_7)$ cycloalkyl, phenylalkyl having 1 to 4 carbons in the alkyl portion, phenyl, pyridyl, pyrimidyl, thiazolyl and oxazolyl,

or R^4 and R^5 are taken together with the nitrogen to which they are attached and form an optionally substituted saturated or unsaturated 5- or 6-membered ring, a saturated or unsaturated 6-membered heterocyclic ring containing two heteroatoms, or a quinoline ring optionally substituted with fluoro,

where said optionally substituted saturated or unsaturated 5- or 6-membered ring may be mono- or di-substituted and each substituent is independently selected from the group consisting of alkyl having 1 to 4 carbons, CO_2R^7 wherein R^7 is as defined below, $CONH_2$, $CON(CH_3)_2$, oxo, hydroxy, NH_2 and $N(CH_3)_2$, and said saturated or unsaturated 6-membered heterocyclic ring containing two heteroatoms has the second heteroatom selected from the group consisting of O, S, NH, NCH_3, $NCOCH_3$ and NCH_2Ph;

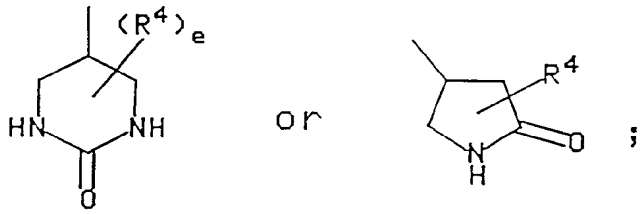
R^7 for each occurrence is independently selected from the group consisting of hydrogen and $(C_1\text{-}C_4)$alkyl;

and R^8 is selected from the group consisting of $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_7)$cycloalkyl, phenyl and phenylalkyl having 1 to 4 carbons in the alkyl portion;

with the proviso that:

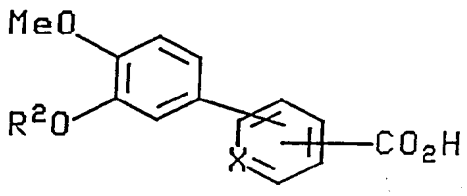
when R^1 is methyl or ethyl; R^2 is $(C_7\text{-}C_9)$polycycloalkyl or indanyl; A, B and Y are covalent bonds; X is N; and R^3 is hydrogen;

then Z is not



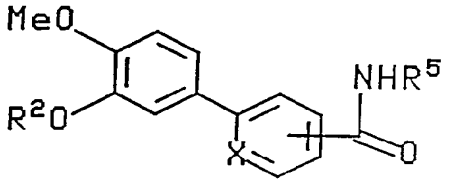
;

when the compound of formula I is



wherein X is CH or N and R^2 is as defined above for formula I, the CO_2H can only be in the para position relative to the bond to the catechol moiety;

when the compound of formula I is



wherein X is CH or N and R^2 and R^5 are as defined above for formula I, the amide can only be in the para or meta position; and the compound of formula I cannot be *trans*-1-[4-[2-[3(cyclopentyloxy)-4-methoxy-phenyl]-ethenylphenyl]-2-methyl-1H-imidazo[4,5-c]-pyridine, for the manufacture of a medicament for inhibiting production of TNF (tumour erosis factor).

2. A use according to claim 1 wherein R1 is methyl or difluoromethyl; R^2 is $(C_3\text{-}C_7)$cycloalkyl, $(C_6\text{-}C_9)$polycycloalkyl, phenylalkyl, phenoxyalkyl or indanyl,

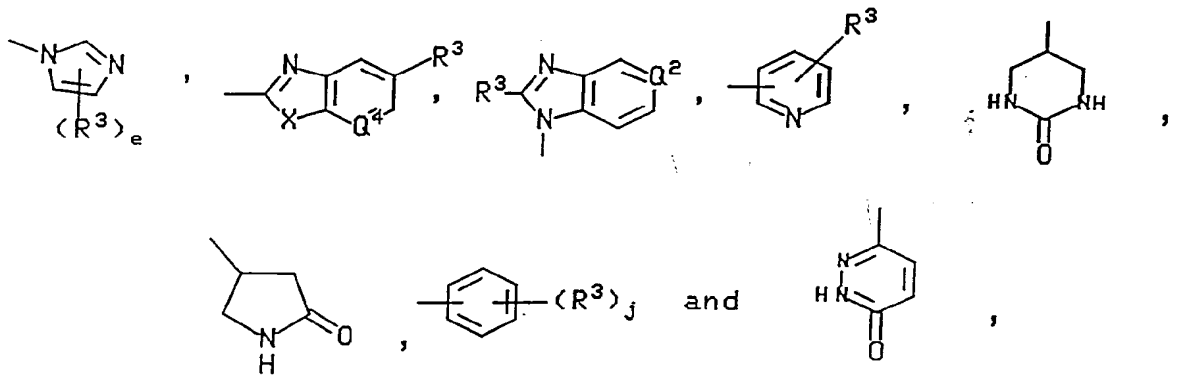
where the alkyl portion of said alkyl, cycloalkyl, polycycloalkyl, phenylalkyl, phenoxyalkyl and indanyl may

optionally be substituted with one or more fluorine atoms, -OH or (C_1-C_4)alkoxy,

and the aryl portion of said phenylalkyl, phenoxyalkyl and indanyl may optionally be substituted with (C_1-C_4) alkyl, (C_1-C_4)alkoxy or halogen.

3. A use according to claim 2 wherein A and B are independently selected from the group consisting of a covalent bond, (C_1-C_5)alkylene, (C_2-C_5)alkenyl and phenylene; and Y is a covalent bond or O.

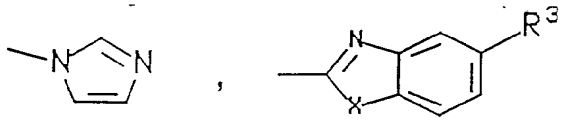
4. A use according to claim 3 wherein A is a covalent bond, methylene or cis-ethenyl; B is a covalent bond or phenylene and Z is selected from the group consisting of



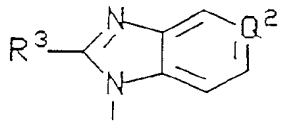
wherein j is 1 or 2; Q^4 is CH or N and Q^2 is CH or N.

5. A use according to claim 4 wherein R1 is methyl; R^2 is cyclopentyl, norbornyl, indanyl, 1-phenylbut-3-yl, 1-phenoxyeth-2-yl, 1-phenylhex-5-yl or 1-phenylpent-4-yl; R^3 is (C_1-C_4)alkyl, CO_2H, $CONH_2$, nitro, $NHSO_2Me$, CF_3 or hydrogen; and e is 1.

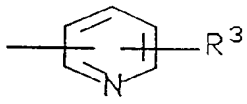
6. A use according to claim 5 wherein Z is selected from the group consisting of



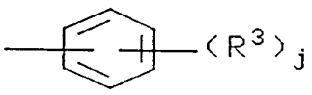
wherein R^3 is H, CO_2H or $CONH_2$,



wherein R^3 is (C_1-C_6)alkyl,



wherein R^3 is H, CO_2H or $CONH_2$, and

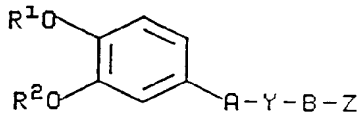


wherein R^3 is (C_1-C_6)alkyl, H, CO_2H, $CONH_2$ CF_3, NO_2 or $NHSO_2Me$.

7. A use according to any one of the preceding claims, which is for the manufacture of a medicament for treating or alleviating an inflammatory condition or disease, sepsis, septic shock, tuberculosis, multiple sclerosis and other autoimmune diseases, graft versus host disease or cachexia associated with AIDS or cancer in a mammal.

8. A use according to claim 7 wherein the inflammatory disease or condition is rheumatoid arthritis, osteoarthritis, asthma, bronchitis, chronic obstructive airways disease, psoriasis, allergic rhinitis, dermatitis or inflammatory bowel disease.

9. A pharmaceutical composition comprising a pharmaceutically acceptable diluent or carrier and a tumor necrosis factor inhibiting amount of a compound selected from the group consisting of compounds of the formula (I)



,

(I)

the racemic-diastereomeric mixtures and optical isomers of said compounds and the pharmaceutically acceptable salts thereof as defined in any one of claims 1 to 6, together with instructions for the use thereof for the treatment or alleviation of a condition as defined in claim 7 or 8.

10. Commercial package containing a compound of the formula (I), racemic- diastereomeric mixture or optical isomer or pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 6 in a form suitable for oral or parenteral administration, together with or bearing instructions for the use thereof in treating or alleviating a condition as defined in claim 7 or 8.